TO MEASURE RETINAL NERVE FIBRE LAYER THICKNESS IN TRANSFUSION DEPENDENT THALASSEMIA PATIENTS

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DECLARATION BY THE CANDIDATE

I hereby declare that the thesis entitled **"TO MEASURE RETINAL NERVE FIBRE LAYER THICKNESS IN TRANSFUSION DEPENDENT THALASSEMIA PATIENTS"** submitted towards partial fulfillment of the requirements for the award of MS in Ophthalmology degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Sumeet Chopra**, Former Professor & Head, Department of Ophthalmology, **Dr. Shruti Kakkar**, Associate Professor, Department of Paediatrics and **Dr. Ritesh Verma,** Assistant Professor, Department of Ophthalmology. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

my family

&

Teachers

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LIST OF ABBREVIATIONS

TDT- Transfusion Dependent Thalassemia

CNV- Choroidal neovascularisation

Hb – Haemoglobin

RNFL- Retinal nerve fibre layer

OCT – Optical coherence tomography

LIC – Liver iron concentration

DFO -Deferoxamine

DFP - Deferiprone

DFX- Deferasirox

RPE- Retinal pigment epithelium

TBUT- Tear film break up time

PXE- Pseudoxanthoma elasticum

CNV-Choroidal Neovascularization

IDA- Iron deficiency anaemia

SCD- Sickle cell disease

CMT- Central macular thickness

GLT- Ganglion layer thickness

ABSTRACT

Introduction

Transfusion-dependent thalassemia is an inherited disorder requiring lifelong transfusion and chelation therapy. The retinal nerve fibre layer (RNFL) is susceptible and can be impacted by anaemia-induced hypoxia. Timely detection of RNFL thinning is crucial in preventing severe complications. Optical coherence tomography (OCT) can provide precise ā measurements of RNFL thinning, aiding in identifying retinal layer thinning in thalassaemic patients. This study aimed to evaluate the thinning of the RNFL in thalassaemicpatients and its correlation with systemic parameters.

Aims and objectives

1. To measure the retinal nerve fibre layer thickness using OCT in transfusion-dependent thalassemia patients.
2. To compare retinal nerve fibre thickness in thalassemia patients to that of normal subjects.
3. To correlate the thinning with systemic parameters.

Material and methods

This cross-sectional study included 85 patients with transfusion-dependent thalassemia (170 eyes) and 85 healthy controls (170 eyes). All participants underwent a standard ophthalmological examination, followed by CIRRUS HDOCT 6.5 (Carl Zeiss) imaging to assess retinal nerve fibre layer thickness and other parameters. Various systemic parameters were then recorded and compared with the ocular parameters.

Results

We found no significant thinning of RNFL in TDT patients and no correlation was found with various systemic parameters. However, we found reduced tear film break up time and Schirmer test values in TDT patients suggesting dry eye in TDT patients.

Conclusion

We found no RNFL thinning in TDT patients and no correlation with systemic parameters contrary to the previous studies.

Key words: Transfusion dependent thalassemia, Retinal nerve fibre layer thickness, Optical coherence tomography, Ganglion layer thickness, central macular thickness.

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INTRODUCTION

Thalassemia is a hereditary illness resulting from insufficient or no globin chain formation during the synthesis of haemoglobin (Hb). Decreased synthesis of the beta-globin chain in Hb and a quantitative decline in Hb production are the characteristics of this disorder.[1]

Based on the clinical severity and the patient's requirement for frequent blood transfusions, thalassemia disorders are categorized as either transfusion-dependent (TDT) or non-transfusion-dependent thalassemia (NTDT). [2] For TDT patients to live, regular transfusions are necessary. [2] In contrast, people with NTDT do not need frequent transfusions but they could need them on occasions such as stress, pregnancy or an infection. [3]

CLINICAL DIAGNOSIS

Severe anaemia (Hb levels below 7 g/dL), pallor, jaundice, irritability, feeding problems, failure to thrive, skeletal abnormalities, and abdominal enlargement due to hepatosplenomegaly in the absence of proper transfusion are common symptoms seen in patients with TDT. Long bone anomalies and abnormalities of the craniofacial structure, such as frontal bossing, malar prominence, a depressed nasal bridge, maxillary hypertrophy, and osteoporosis, are examples of skeletal alterations. [4, 5]

COMPLICATIONS

The excess iron in TDT patients saturates the available transferrin and circulates as free non-transferrin bound iron leading to the formation of free radicals and tissue damage. Iron accumulation preferentially occurs in parenchymal tissues such as the heart, liver, and endocrine glands. Cardiovascular (CV) complications secondary to iron overload are the leading cause of death in patients with thalassemia, encompassing both TDT and NTDT. [6-8] Liver disease in this subgroup primarily results from iron overload and viral hepatitis, leading to chronic inflammation, fibrosis, and ultimately cirrhosis.[9,10] Iron buildup

in endocrine glands can lead to various disorders, such as hypothyroidism, hypoparathyroidism, adrenal insufficiency, diabetes mellitus, and hypogonadism.[11]

Hence, adherence to iron chelation therapy is the most important predictor of morbidity and mortality. There are mainly three classes of chelation available: deferoxamine (DFO), deferiprone (DFP) and deferasirox (DFX). Chelation is usually started at about 2 years of age,serum ferritin >1000 ng/ml,or when 10 transfusions have been given. Thus, adequate chelation therapy can maintain adequate liver iron concentrations (LIC), prevent hepatic fibrosis and CV disease, and help in adequate normal and sexual development. [11]

OCULAR MANIFESTATIONS OF BETA THALASSEMIA

Ocular manifestations in TDT may be related to the chelating drugs that are utilized, iron overload, or the disease itself. Ocular surface conditions, lens opacities, and retinal pigment epithelium [RPE] degeneration are examples of ocular manifestations. [12]

OCULAR SURFACE DISEASE

The lacrimal glands, which are tubuloacinar exocrine glands organized similarly to the salivary glands, are often affected in patients with TDT. The increased iron deposition in glands has a cytotoxic effect, primarily causing secretory dysfunction.[13]

Ocular surface disease in TDT patients is characterized by the loss of goblet cells and the transformation of conjunctival cells into a squamous form. This transformation may be associated with a decrease in antioxidants. Significant reductions in tear film parameters, including tear film break-up time(TBUT), Schirmer test results, and Rose Bengal staining, have been reported.[14,15]

ANTERIOR SEGMENT ABNORMALITIES

According to multiple studies, children with TDT have severe growth retardation that affects both ocular and general growth (as seen by reduced vitreous chamber depth and shorter axial length). Though, it

hasn't been proven that differences in ocular growth and biometric parameters and general growth retardation are directly related. It is postulated that emmetropia is likely achieved by compensatory biometric changes such as steeper corneas and larger lenses, which counteract the refractive disadvantages of shallower vitreous chamber depth and shorter axial length. As a result, there is no discernible difference in the mean spherical equivalent between the two groups and variations in refractive status and visual acuity between healthy controls and TDT patients. [16]

In children with TDT, lens opacities significantly contribute to decreased visual acuity and can obstruct vision if they develop near the visual axis. [12] In patients with TDT, lens opacities may be caused by iron overload and the resulting oxidative damage to the lens. This condition disrupts the balance between oxidants and antioxidants, and iron-chelating agents may also play a role.[17,18] DFP due to its small molecular size can cross the blood-ocular barrier and can get deposited in the aqueous humour where it inhibits glutathione peroxidase enzyme leading to cataract formation.[19,20]

FUNDUS ABNORMALITIES

Fundus changes in TDT are common, age-dependent, and similar to those observed in Pseudoxanthoma elasticum (PXE): central pattern dystrophy-like changes, comet tail lesions in the periphery, and a peau-d'orange" look encircling the periphery. [17, 21, 22] Drusen in the optic disc are also commonly found. It is known that these modifications, especially pattern dystrophy-like changes and angioid streaks, predispose people to major vision-threatening conditions like Choroidal Neovascularization (CNV). Apart from the PXE-like condition, retinal vascular tortuosity may be another disease manifestation linked to the degree and duration of anemia. [23]

DESFERRIOXAMINE RETINOPATHY

DFO can cause opacification or loss of transparency in the RPE in addition to degeneration in other places, either separately or in

combination, including the foveo-macular, macular, paramacular, papillary, peripapillary, and peripheral areas. There may also be RPE pigment changes, optic disc enlargement, and optic nerve damage.[24,25]

The ocular side effects noted for DFX are cataracts, lenticular opacities, retinal disorders, elevations in IOP. [26]

Due to excellent advancements in the management of thalassemia and increased life expectancy newer emerging complications are being identified in patients with thalassemia. But there exists paucity in research associated with ocular manifestations of this disease, especially retinal nerve fibre layer.

This thesis aims to address the aforementioned gap in knowledge by systematically evaluating retinal nerve fibre layer thickness (RNFL) in thalassemia patients using non-invasive imaging methods such as optical coherence tomography (OCT). The study will encompass a comprehensive assessment of RNFL thickness across different stages of thalassemia severity and explore potential correlations with clinical parameters, including Hb levels, transfusion frequency, and chelation therapy.

AIMS AND OBJECTIVE

1. To measure the retinal nerve fibre layer thickness using OCT in transfusion dependent thalassemia patients.
2. To compare retinal nerve fibre thickness in thalassemia patients to that of normal subjects.
3. To correlate the thinning with systemic parameters.

REVIEW OF LITERATURE

Children with TDT typically present before their first year of life.[27] It is estimated that only 11.7% of TDT patients receive proper transfusions, and of those, only 39% have access to adequate iron chelation therapy, with many succumbing to complications from uncontrolled iron overload.[28] This issue is primarily due to the high costs and limited availability of treatment. However, through the collaborative efforts of medical professionals, improved government programs, and support from welfare organizations, the life expectancy of TDT patients has significantly improved. Consequently, these patients deserve better vision care.

The research associated with RNFL measurement in TDT patients was pioneered by Aksoy et al.[29] in 2014. In his research, he took into account 47 children with TDT, 22 children with iron deficiency anaemia and 35 healthy controls. RNFL thickness was measured in all study subjects using OCT. He in his study reported, significant ($p<0.01\%$) thinning in all quadrants in TDT patients compared to two groups and significant ($p<0.001$) thinning in inferior quadrants in IDA group compared to controls.

OPTICAL COHERENCE TOMOGRAPHY

OCT utilizes light waves to generate a reflectivity versus depth profile of the tissue under examination. [30] A broadband light source is divided into two beams: a sample beam that is focused on the subject's retina and a reference beam that follows a predetermined route. Retinal structures' light reflections obstruct the reference beam, which has followed a predetermined delay path. The measurement of light reflections versus delay or depth is done using this interference. Earlier OCT systems, such as Stratus OCT, produced axial scans (A-scans) at a rate of 400 A-scans per second with an axial resolution of 8µm to 10µm by mechanically scanning the reference mirror position and delay to measure echoes from different depths sequentially. This method was known as time-domain detection. [31]

Fourier domain detection in the form of spectral domain OCT has recently been made commercially available on a number of OCT devices. An interferometer equipped with a high-speed spectrometer detects light reflections from all time delays simultaneously in spectral domain optical coherence tomography (SD-OCT). Light reflections can be simultaneously detected by measuring and Fourier processing the interference spectrum, negating the need for mechanical scanning of the reference mirror. Significant gains in signal-to-noise ratio and image acquisition speed are made possible by this enhanced sensitivity.[32] With improvements in light sources, commercially available SD-OCT systems can attain axial scanning speeds between 27,000 and 68,000 A-scans per second, with an axial resolution of 5 to 7 µm in the eye.

A 3.45 mm diameter circle centred on the optic disc is scanned at a speed of 32 frames per second to provide three continuous RNFL thickness measurements. The software evaluates and shows the image quality on the OCT screen following each measurement. To generate a single RNFL thickness value, the three measurements that pass the quality test are averaged. We employ the mean RNFL thickness, the lowest and maximum RNFL thickness, and the RNFL thickness in each of the four disc quadrants (superior, nasal, inferior, and temporal) for each study eye. [33]

CARL-ZEISS HD-OCT

Imaging Model 5000 The Carl-Zeiss HD-OCT Model 5000 utilizes SD-OCT technology, featuring a Super luminescent diode (SLD) with an 840 nm optical source. With a depth of 2.0 mm in tissue at 1024 points and a scan speed of 27,000–68,000 A-scans per second, it offers an axial resolution of 5 µm and a transverse resolution of 15 µm in tissue.Using an SLD of 750 nm as the optical source, line scanning ophthalmoscopy (LSO) is employed to obtain a live fundus image during alignment and the OCT scan.

With many companies producing various SD-OCT instruments, conducting multicentre clinical trials can be challenging due to

differences in hardware, segmentation algorithms, and analysis software. This variation complicates the comparison of values between systems. Research indicates that physicians have to exercise caution when comparing thickness readings from several OCT brands that belong to the same generation, as variations in acquisition methods may impact the outcomes. This often poses a dilemma for providers considering switching from one OCT model to another when baseline data has already been collected on established patients. According to recent research, while repeatable OCT results are typical in healthy people, variations in acquisition and border recognition between machines may lead to inconsistent findings when retinal disease is present.[34]

Few years later, Uzun et al.[35] conducted similar research, he compared 47 TDT patients with 51 healthy controls. His results were in conjunction with Aksoy et al.[29], as he also reported significant RNFL thinning in all quadrants. He additionally tried to correlate RNFL thinning with parameters with age, Hb and serum ferritin levels but no significant correlation was found.

Ulusoy et al.[36] conducted a study in turkey, where he considered 32 TDT patients, 34 sickle cell disease(SCD) patients and 44 healthy controls. He tried comparing various OCT parameters among groups such as RNFL thickness, choroidal thickness, central macular thickness (CMT) and ganglion cell layer thickness (GLT). In his study, he could find significant RNFL thinning in SCD patients but no significant RNFL thinning was noted in TDT patients. He concluded that sub- foveal choroidal thickness was significantly higher in controls than patients with SCD and TDT. Similarly, significant GLT thinning was noted in SCD patients but no significant thinning was noted in TDT patients. CMT showed no significant variation among various groups.

Datta et al [37] conducted a study in eastern India, where he included 150 study subjects, out of which 99 subjects had thalassemia, 33 had IDA and rest had chronic anaemia. On comparing RNFL thickness in

various groups, he found significant thinning in all quadrants with nasal quadrant, followed by temporal, inferior, and superior quadrants in thalassemia patients. They correlated the RNFL thinning with Hb levels, and interestingly they found positive corelation with mean Hb levels and RNFL thinning, such that more anaemic patients had more severe RNFL thinning.

Basiony et al.[38] conducted a study including 15 patients with TDT and 15 healthy controls. In his study he reported significant thinning in nasal superior, nasal inferior and nasal sectors in TDT patients. RNFL thinning was correlated with Hb and serum ferritin levels. Nasal superior sector correlated significantly with serum Hb levels while temporal superior and nasal sectors correlated with ferritin levels.

Haghpanah et al.[39] recently conducted a cross sectional study, where he took into account 39 patients with TDT and compared them with 27 age and sex matched healthy controls. He considered measuring RNFL thickness along with central macular thickness and again compared it with age matched controls.

Contrary to previously conducted studies, he reported thinner CMT and macular thickness in various quadrants in TDT patients as compared to controls ($p<0.05$). He also reported a negative correlation between Hb and CMT. Though he reported no significant thinning of RNFL in TDT patients.

Bayramoglu et al.[40], conducted a cross sectional study to analyse the posterior segment changes in the children with TDT. He compared 44 TDT patients with 44 age and gender matched controls. He subjected the patients to complete ophthalmological examination followed by OCT.

Various parameters like CMT, GLT, RNFL thickness, sub foveal choroidal thickness, choroidal thickness (temporal to fovea, nasal to fovea, temporal to optic nerve head, nasal to optic nerve head) were compared between cases and controls. This study found no significant difference between two groups in terms of RNFL, CMT and GLT. However, they reported significant thinning in sub foveal, perifoveal and peripapillary choroidal thickness.

AttaAllah et al.[41] in his study, compared optical coherence tomography angiography (OCT-A)findings between the patient and control groups. The thalassemia group was further subdivided into two groups to study OCTA findings according to their ferritin level (value <2500 ng/ml)

The foveal avascular zone (FAZ) was significantly larger in thalassaemic patients compared to controls at both the superficial and deep vascular network levels. Furthermore, thalassemia patients with serum ferritin levels of 2500 ng/ml or higher exhibited a significantly larger deep FAZ area than those with serum ferritin levels below 2500 ng/ml. The underlying pathophysiology for the enlargement of the FAZ and the more pronounced changes in the deep capillary plexus is that the FAZ area is the most vulnerable and distant part of the retinal capillary network. However Kazanci et al[42] did not find such significant changes in the FAZ area.

Georgalas et al [43] colleagues used OCTA in a recent study to assess certain shape descriptors of FAZ area on 27 thalassemia patients and 23 healthy controls. They discovered that there were no appreciable variations in the FAZ region sizes in the deep and superficial retinal plexuses.

To understand tear film parameters in TDT**,** Gartaganis et al [14] compared 52 TM patients and 22 normal subjects in terms of Schirmer tests, TBUT, and conjunctival cytology. They found that

46.15% of the TDT patients had TBUT values less than 10 seconds, and 56.73% had Schirmer test results below 10 mm. In the control group, 27.27% had TBUT values less than 10 seconds and Schirmer values were less than 10 mm in 36.36%.

The standard Schirmer test with topical anaesthesia can be used to assess tear secretion. To perform the test, the conjunctiva and cornea are first anesthetized with 0.5% proparacaine HCl. Standardized filter paper strips are positioned into the cul-de-sac, away from the cornea, at the intersection of the middle and lateral third of the lower eyelid edge after a minute. These strips are left in place for 5 minutes. Patients are asked to look straight ahead and blink regularly during the test, which is performed in a dimly lit environment. Values of less than 8 mm of moistened filter paper within 5 minutes (measured from the fold) are considered subnormal.

The inferotemporal conjunctival sac is stained with fluorescein that has been soaked with a preservative-free tear solution to perform the standard TBUT measurement. The participants are directed to move their eyes and blink multiple times to fully incorporate the fluorescein into the tear film. Subsequently, they are instructed to shut their eyes and then open them. The amount of time that passes between the final full blink and the emergence of the first dark spot in the tear fluorescein layer is measured using a digital timer. For every eye, three different readings are obtained, and the average of these values is determined. TBUT values of less than 10 seconds are considered abnormal.[44]

Conjunctival cytology using a cytobrush was which was suggestive of goblet cell loss and squamous metaplasia. Deficiencies in trace elements and vitamins were suggested as a possible mechanism for inducing conjunctival damage. Goblet cell loss in the conjunctiva and a noticeable reduction in microvilli and microplicae in the cornea and conjunctiva are the results of deficiencies in zinc, copper, magnesium, and vitamins A, C, and E.

Another potential cause of conjunctival alterations could be peroxidative damage, which can be brought on by either an excess of UV radiation or a deficit in vitamin E. Patients with thalassemia are

particularly vulnerable to UV-induced peroxidative tissue damage because of the secondary iron excess brought on by ongoing infusions of blood. It has been suggested that oxidative stress and reactive oxygen species production are elevated in thalassemia patients with iron overload.

Jafari et al [45], in his study compared 54 TDT patients with 56 healthy controls. He did complete ophthalmological examination in subjects and compared them for visual acuity, refraction testing, slit lamp examination, fundoscopy, tonometry, perimetry, TBUT, colour vision. The study found no significant differences in the spherical equivalent between thalassemia patients and normal subjects. However, they reported that 10.2% of thalassemia patients had peripheral cortical cataracts. Additionally, 16.7% of thalassemia patients showed RPE degeneration. Visual field evaluations of 33.7% of thalassemia patients showed abnormalities, with overall depression (17.3%) being the most common. Only two thalassemia patients had colour vision deficiencies, specifically red-green deficiency. The data indicated a statistically significant increase in IOP among thalassemia patients compared to controls, which was hypothesized to result from iron overload in the trabecular meshwork. They also noted reduced TBUT in thalassemia patients and found a correlation with ferritin levels.

Thus, there lies a lot of variation in various parameters across various studies.

MATERIAL AND METHODS

This study was conducted in the Department of Ophthalmology, Dayanand Medical College and Hospital, Ludhiana in which 170 eyes of 85 thalassemia patients registered and undergoing treatment in the Thalassemia Day Care Centre of the Department of Paediatrics were analysed on various systemic and ocular parameters and compared with 170 eyes of 85 healthy controls. Prior approval from the Institutional Review Board of the institute was taken. This study was conducted in accordance with the tenets of the Declaration of Helinski for research involving human subjects.

SOURCE OF DATA

TYPE OF STUDY-Cross sectional study with case and control groups

STUDY POPULATION- To calculate the sample size of the study

The formula used is as under:

$n = (\sigma 12 + \sigma 22) (Z\alpha + Z\beta)^2 / (m1 - m2)^2$

Where,

Zα = Value of standard normal variate corresponding to α level of significance (1.96)

Zβ = The standard normal deviate for desired power (0.842)

m = mean

σ = Standard deviation

Assumptions:

From the study conducted by UZUN ET AL

Mean Group (m1) = 94

Mean Group (m2) = 100

Coefficient of variation = 150%

Standard deviation Group (σ1) = 10

Standard deviation (σ2) = 17

With the above assumptions the sample size for 95% confidence level & 80% power works out 85 in each group

HENCE CASE GROUP-85 CONTROL GROUP-85

INCLUSION CRITERIA-

1. Any patient willing to participate in the study.
2. Transfusion dependent thalassemia at thalassemia day care centre, Dayanand medical college, Ludhiana.
3. Age between 5 and 30 years of age.
4. Patients cooperating for OCT.

EXCLUSION CRITERIA-

1. Children with history of retinal diseases.
2. Children with diabetes mellitus.
3. Children with history of any intraocular surgery.
4. Children with optic disc disorders.
5. Children with history of retinopathy of prematurity.

METHODS OF COLLECTION OF DATA

All subjects underwent comprehensive ophthalmic evaluation which included visual acuity measurement by Snellen's chart, slit lamp examination, non-contact tonometry, and fundus examination by indirect ophthalmoscopy. Before testing, the pupil of each subject was dilated by instillation of 1% tropicamide and 2.5% phenylephrine hydrochloride to the eye three times over a 10 minutes period. Peripapillary RNFL thickness was measured using ZEISS CIRRUS OCT machine.

PRINCIPLE OF OPTICAL COHERENCE TOMOGRAPHY

OCT is a quick, non-invasive and reproducible imaging tool for macular lesions and has become an essential part of clinical practice.

OCT is an optical analogue of ultrasound imaging that uses low coherence interferometry to produce cross-sectional images of the retina. It captures optical scattering from the tissue to decode spatial details of tissue microstructures. It uses infrared light from a super-luminescent diode that is divided into two parts: one of which is reflected from a reference mirror and the other is scattered from the

biological tissue. The two reflected beams of light are made to produce interference patterns to obtain the echo time delay and their amplitude information that makes up an A-Scan.

A minimum pupil diameter of 3 mm is required to obtain a good OCT image. An appropriate scanning protocol is selected to scan the retinal area of interest and a live OCT window is seen. The patient is instructed to look at the internal target at the centre (for macular scanning) or an external target where appropriate. Once the fundus image on the monitor is focused, the OCT image appears on the monitor, focus is enabled by correcting refractive errors. The saved OCT scans are analysed both qualitatively and quantitatively. The OCT view window consists of the analysed OCT images with its corresponding fundus image showing the orientation of the OCT scan. The analysis report varies with different OCT systems. Warm colours indicate thicker retinal areas and cool colours indicate thinner retinal areas.

The subject was seated and aligned properly, three 200x 200-cube optic disk scans were obtained per eye, scans with poor signal strength were discarded, and new one was obtained. All scans were performed by a single operator. The average RNFL thickness, the average thickness in the four sectors — superior, inferior, temporal and nasal and the average thickness in all clock hour positions was recorded. The superior clock hour was 12 o'clock, and the others were assigned accordingly in a clockwise manner in the right eye and counterclockwise in the left.

OUTCOME

Outcome was measured in terms of RNFL thickness, CMT, GCL thickness, TBUT and Schirmer test values.

STATISTICAL ANALYSIS

Data was described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. To determine whether the data is normally distributed, a Kolmogorov-Smirnov test was used. Comparison of quantitative variables between the study groups was done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square ($\chi 2$) test was performed and fisher exact test was used when the expected frequency is less than 5. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

OBSERVATIONS AND RESULTS

This study was conducted in the Department of Ophthalmology, Dayanand Medical College and Hospital, Ludhiana in which 170 eyes of 85 thalassemia patients registered and undergoing treatment in the Thalassemia Day Care Centre of the Department of Paediatrics were analysed on various systemic and ocular parameters and compared with 170 eyes of 85 healthy controls.

Demographic profile

Age

The mean ± SD age in the case and control groups was 18.29 ± 6.86 and 20.87 ± 3.24 years respectively. The median age in the case group was 18 years with an interquartile range of 13-24 years. The median age in the control group was 21 years with an interquartile range of 20-23 years.

Age (Years)	Group		Wilcoxon-Mann-Whitney U Test	
	Case	Control	W	p value
Mean ± SD	18.29 ± 6.86	20.87 ± 3.24	2616.500	0.002
Median (IQR)	18 (13-24)	21 (20-23)		
Min – Max	6 – 30	7 – 28		

Table 1 - Age profile of cases and controls

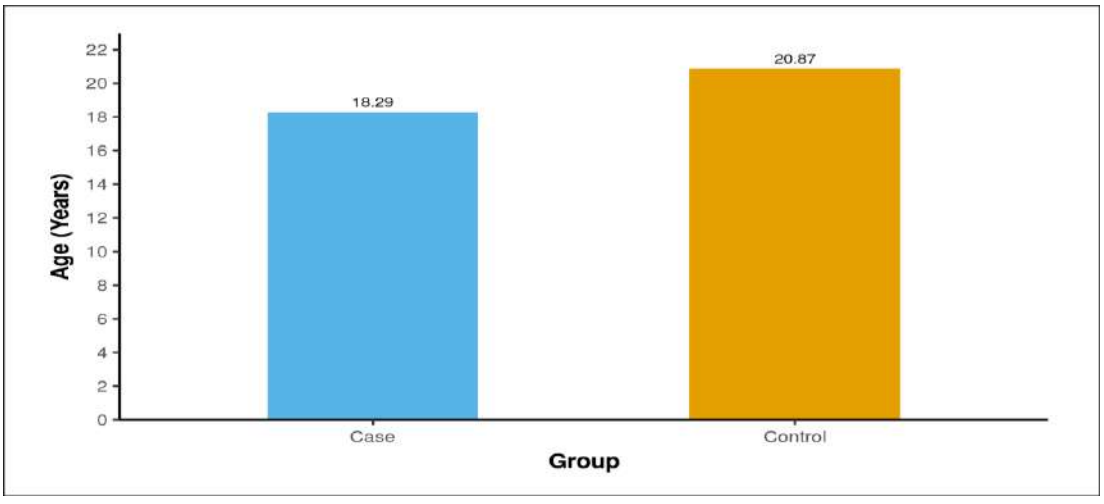

Figure 1-The bar graph depicts the means of age (years) in the cases and controls.

Age at diagnosis

The mean ± SD age at diagnosis in the patients was 23.58± 41.43 months. The median age at diagnosis in the patients was 10 months with an interquartile range of 7-24 months. The age at diagnosis in the patients ranged from 1 – 324 months.

Age At Diagnosis (Months)	
Mean ±SD	23.58 ±41.43
Median (IQR)	10 (7-24)
Range	1 – 324

Table 2- Age of disease diagnosis in cases

Age of initiating transfusion

The mean ± SDof the age of initiating transfusion in the cases was 19.90± 24.76 months. The median age of initiating transfusion in the patients was 9 months with an interquartile range of 6-27 months.

Age Of Initiating Transfusion (Months)	
Mean ± SD	19.89 ± 24.76
Median (IQR)	9 (6-27)
Range	1 – 120

Table 3 - Age of initiating transfusion in thalassemia cases Gender

The case group comprised of 61.2% males and 38.8% females while the control group comprised of 42.4% males and 57.6% females. There was no significant difference between two groups in terms of gender (p=0.014).

Gender	**Group**		**Chi-Squared Test**	
	Case	**Control**	**χ2**	**P Value**
Male	52 (61.2%)	36 (42.4%)	6.031	0.014
Female	33 (38.8%)	49 (57.6%)		
Total	85 (100.0%)	85 (100.0%)		

Table 4- Gender profile.

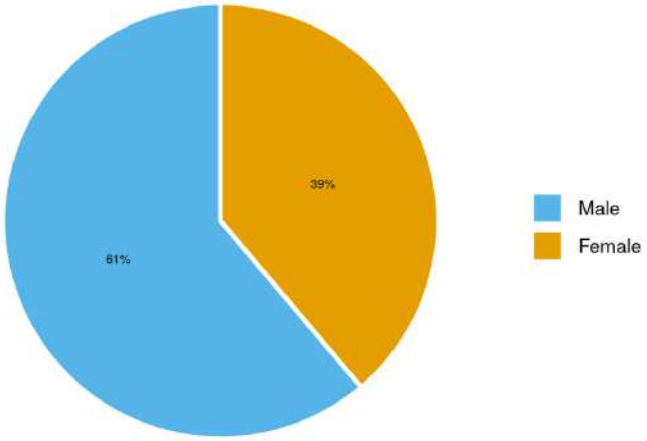

Figure 2 - Gender distribution of cases

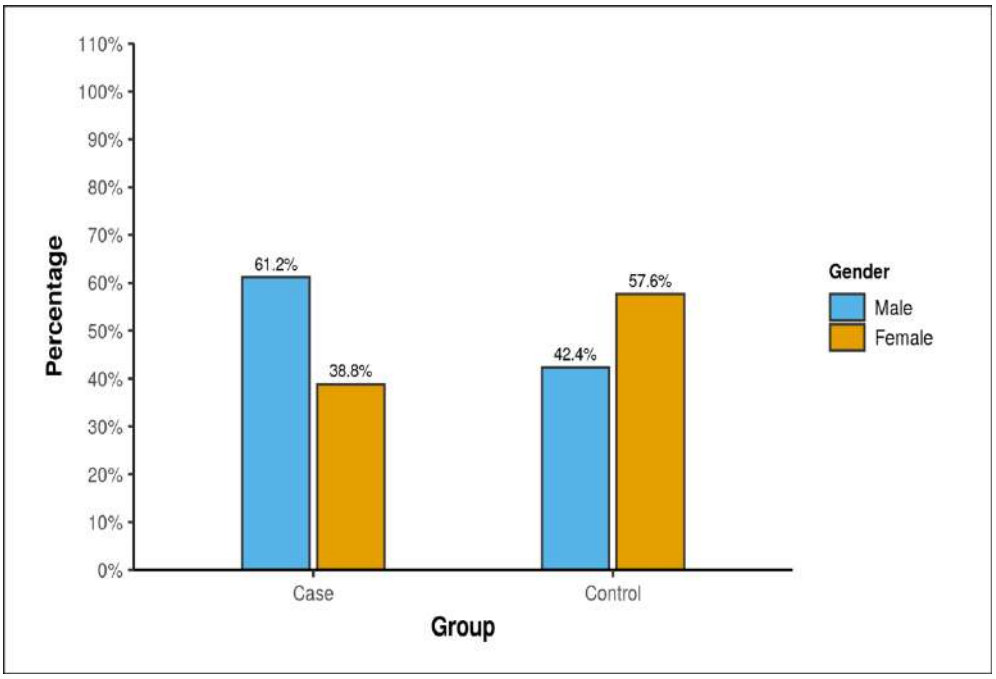

Figure 3 - Distribution of the gender in case and control groups

History of consanguinity

Among the cases, 4 of the patients had history of consanguinity.

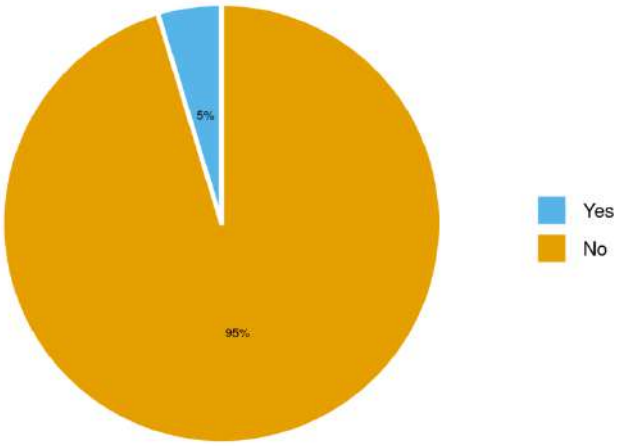

Figure 4 - Distribution of cases on the basis on consanguinity

Education

In the case group, 12.9% of the participants had education up to primary school, 22.4% of the participants had education up to lower secondary,15.3% of the participants had education up to upper secondary and 49.4% of the participants in the case group had higher education.

However, in the control group, 2.4% of the participants had education up to primary school, 3.5% of the participants had education up to lower secondary, 4.7% of the participants in the control group had education up to upper secondary and 89.4% of the participants in the control group had higher education.

Education	**Group**		
	Case	**Control**	**Total**
Primary School	11 (12.9%)	2 (2.4%)	13 (7.6%)
Lower Secondary	19 (22.4%)	3 (3.5%)	22 (12.9%)
Upper Secondary	13 (15.3%)	4 (4.7%)	17 (10.0%)
Higher Education	42 (49.4%)	76 (89.4%)	118 (69.4%)
Total	85 (100.0%)	85 (100.0%)	170 (100.0%)

Table 5 - Education profile of cases and controls

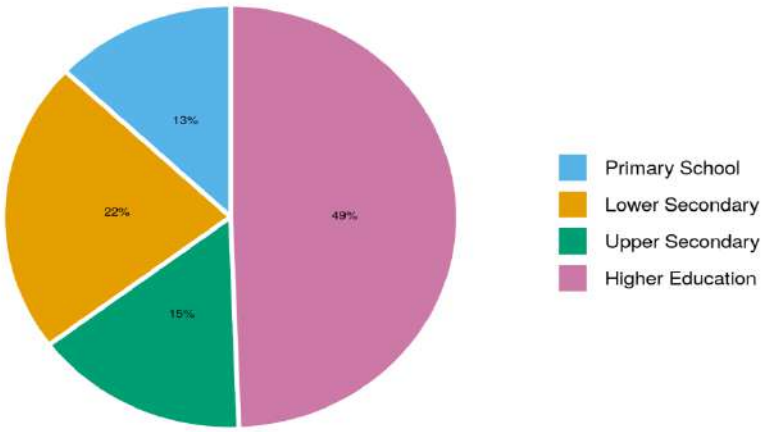

Figure 5 - Distribution of cases in terms of education

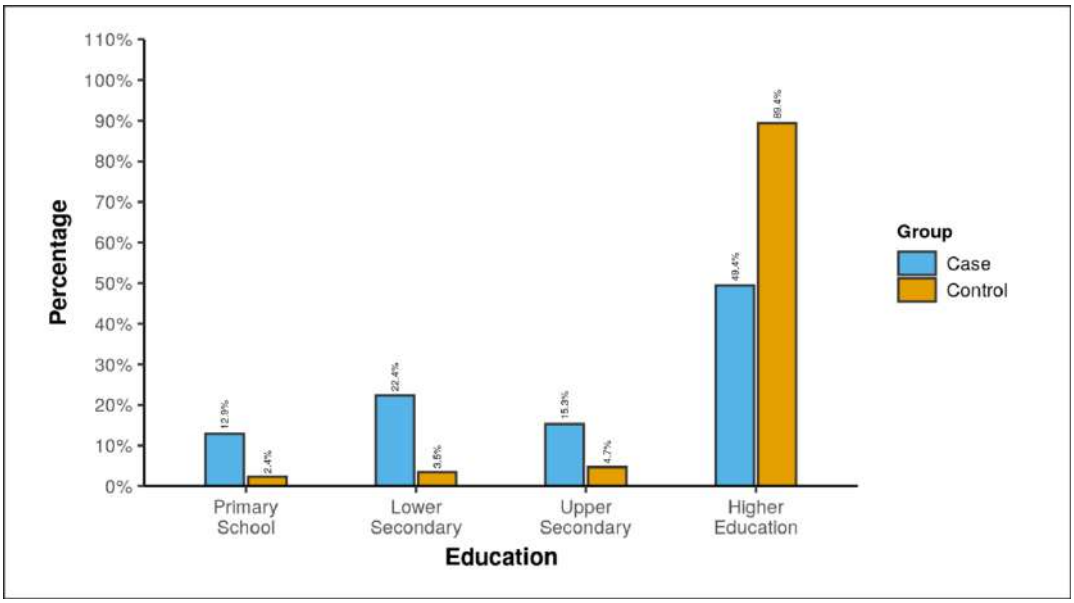

Figure 6- Education status of various study subjects

OCULAR PARAMETERS

Best corrected visual acuity (BCVA)

In the case group, 95.2% of the participants had BCVA of 6/6, while 2.4% of the participants had BCVA of 6/6p another 2.4% of participants had BCVA of 6/9. Contrary to this 100% of the participants in the control group had a BCVA of 6/6. There was a significant difference between the various groups in the distribution of BCVA ($\chi 2 = 8.193$, $p = 0.007$).

BCVA	Group			Fisher's Exact Test	
	Case	Control	Total	χ2	P Value
6\6	162 (95.2%)	170 (100.0%)	332 (97.6%)	8.193	0.007
6\6p	4 (2.4%)	0 (0.0%)	4 (1.2%)		
6\9	4 (2.4%)	0 (0.0%)	4 (1.2%)		
Total	170 (100.0%)	170 (100.0%)	340 (100.0%)		

Table 6 - Distribution of the cases and controls in terms of best corrected visual acuity

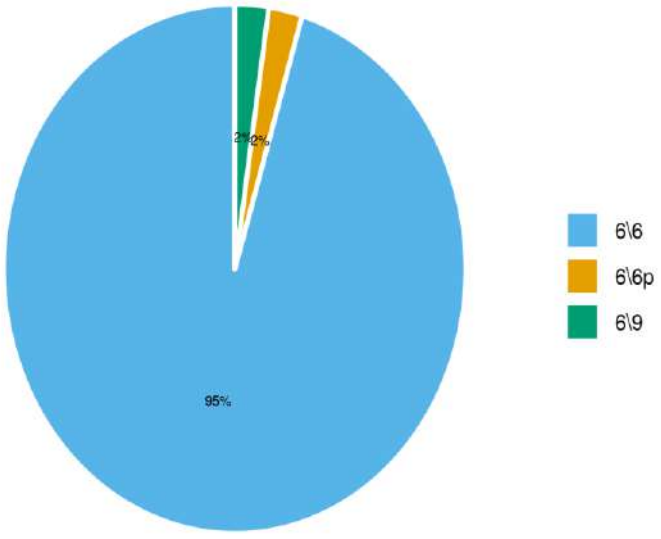

Figure 7- Visual acuity status in cases

Colour vision

In the case group, 97.6% of the participants in the group had normal colour vision, while 2.4% of the participants had red-green defect. However, 98.8% of the participants in the control group had normal colour vision, but 1.2% of participants were noted to have red-green defect. All the 6 patients having colour vision defects were males. There was no significant difference between the various groups in terms of distribution of colour vision ($\chi 2 = 0.679$, $p = 0.685$).

Colour vision	Group			Fisher's Exact Test	
	Case	Control	Total	χ2	P Value
NAD	166 (97.6%)	168 (98.8%)	334 (98.2%)	0.679	0.685
Red-Green Defect	4 (2.4%)	2 (1.2%)	6 (1.8%)		
Total	170 (100.0%)	170 (100.0%)	340 (100.0%)		

Table 7-Distribution of the cases and controls on the basis of colour vision.

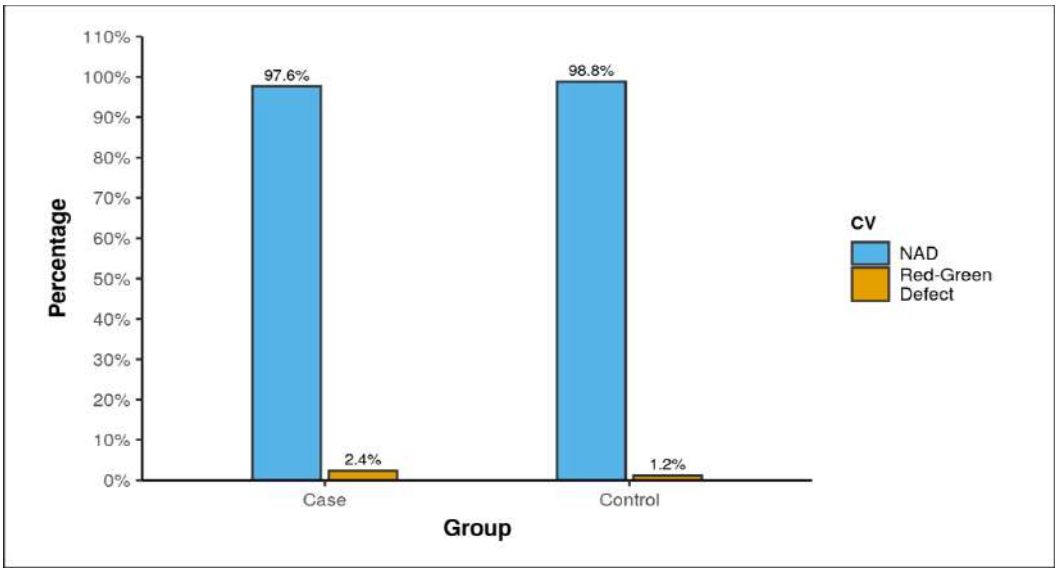

Figure 8 -Distribution of cases and controls on the basis of colour vision

Intraocular pressure

The mean ± SD IOP in the case and control group was 14.03 ±2.34 and 14.59 ±2.81 mm of Hg respectively. The median of IOP in the case group was 14 mm of Hg with an interquartile range of 12-15.75 mm of Hg. The median of IOP in the control group was 16 mm of Hg with an interquartile range of 12-17 mm of Hg. The range of IOP in the case group was from 10 – 21mm of Hg while the IOP in the control group ranged from 9 – 21mm of Hg. There was no significant difference between the groups in terms of IOP (W = 12961.500, p = 0.097).

IOP (mm of Hg)	Group		Wilcoxon-Mann-Whitney U Test	
	Case	Control	W	p value
Mean (SD)	14.03 (2.34)	14.59 (2.81)	12961.500	0.097
Median (IQR)	14 (12-15.75)	16 (12-17)		
Min – Max	10 - 21	9 – 21		

Table 8-Variation of IOP between cases and controls.

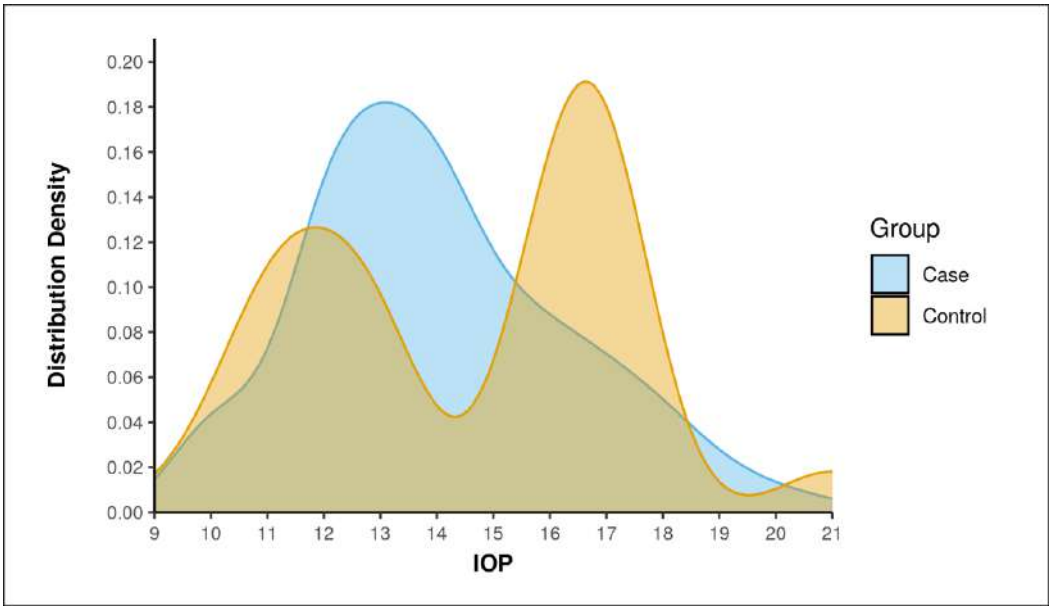

Figure 9 -The density plot depicts the distribution of IOP in the cases and controls.

Tear film break up time (TBUT)

The mean ± SD of TBUT in the case and control group was 6.42±4.40 and 8.41 ±2.14 seconds respectively. There was a significant difference between the 2 groups in terms of TBUT (W = 7168.000, p = <0.001), with the mean TBUT lesser in the case group.

TBUT (seconds)	Group		Wilcoxon-Mann-Whitney U Test	
	Case	Control	W	p value
Mean ±SD	6.42 ± 4.40	8.41 ± 2.14	7168.000	<0.001
Median (IQR)	5 (4-8)	8.5 (7-10)		
Min – Max	1 – 30	3 – 17		

Table 9 - Variation of TBUT between cases and controls.

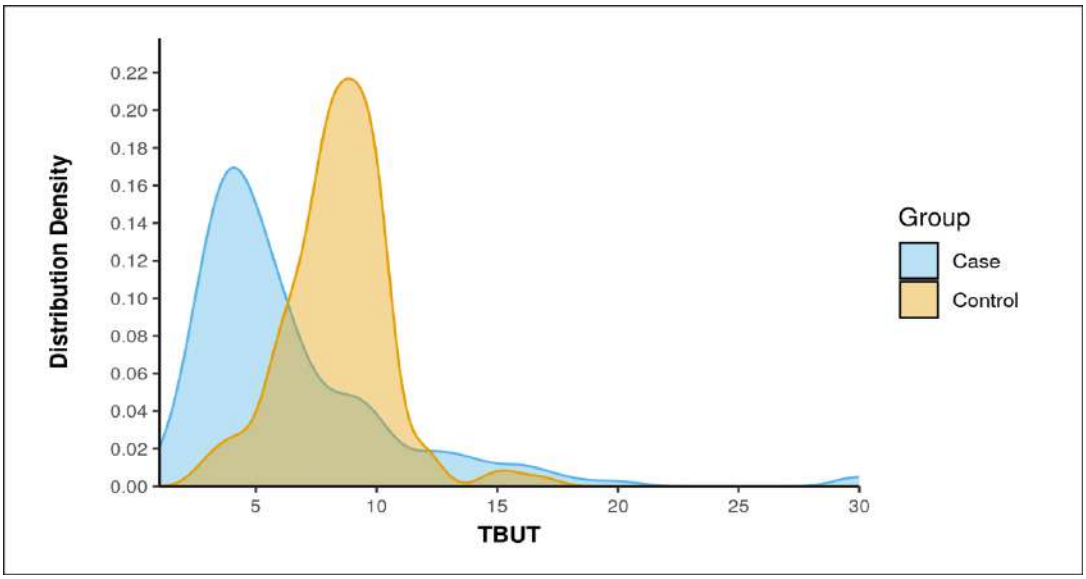

Figure 10 -The density plot depicting the distribution of TBUT in cases and controls.

Schirmer test

The mean ± SD of Schirmer test in the case and control group was 10.91 ±8.44 and 12.74 ±4.49mm respectively. There was a significant difference between the 2 groups in terms of Schirmer test (W = 9746.500, p = <0.001), with the mean value being lower in the case group.

Schirmer test(mm)	Group		Wilcoxon-Mann-Whitney U Test	
	Case	Control	W	p value
Mean ±SD	10.91 ±8.44	12.74 ± 4.49	9746.500	<0.001
Median (IQR)	8 (5-14)	12 (9-16)		
Min – Max	1 – 35	5 – 25		

Table 10-Variation of Schirmer test parameters between cases and controls.

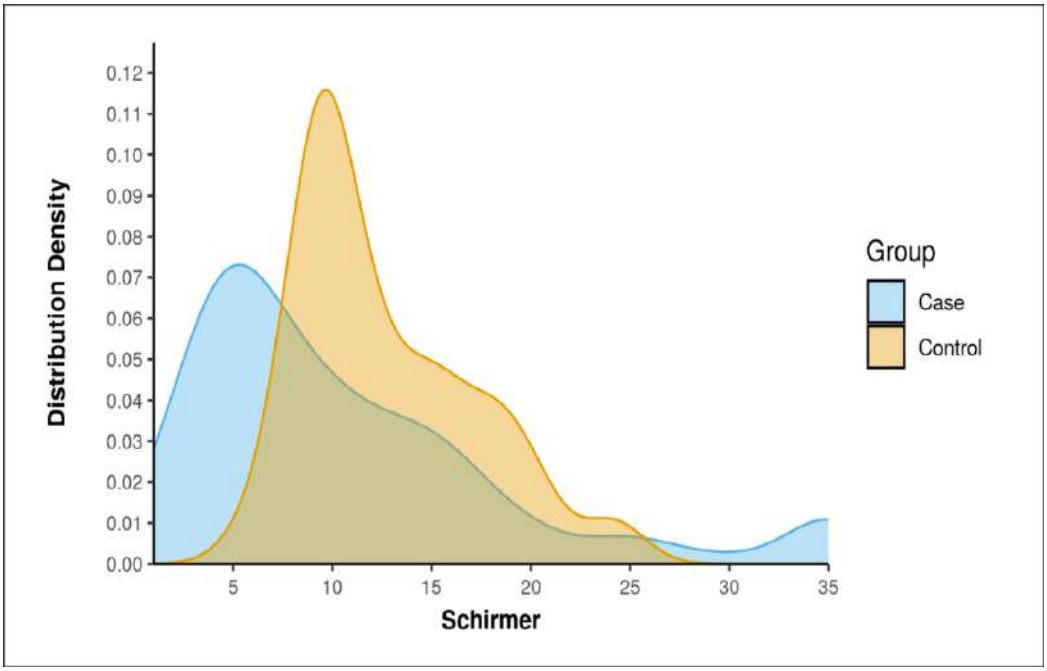

Figure 11 - The density plot depicting the distribution of Schirmer test values between cases and controls.

Central macular thickness (CMT)

The mean ± SD of CMT in the case and control group was 237.11 ± 23.94 and 236.81 ±21.35µm respectively. The median of CMT in the case group was 236µm with interquartile range of 220.25-249µm. The median of CMT in the control group was 241µm with interquartile range of222-252µm. The CMT in the case group ranged from192 - 323µm. The CMT in the control group ranged from 185 – 299µm.There was no statistically significant difference between the groups in terms of CMT (W = 13830.500, p = 0.495).

CMT (µm)	Group		Wilcoxon-Mann-Whitney U Test	
	Case	Control	W	p value
Mean ±SD	237.11 ±23.94	236.81 ±21.35	13830.5	0.495
Median (IQR)	236 (220.25-249)	240.5(222-252)		
Min – Max	192 – 323	185 – 299		

Table 11– Variation of various parameters between cases and controls.

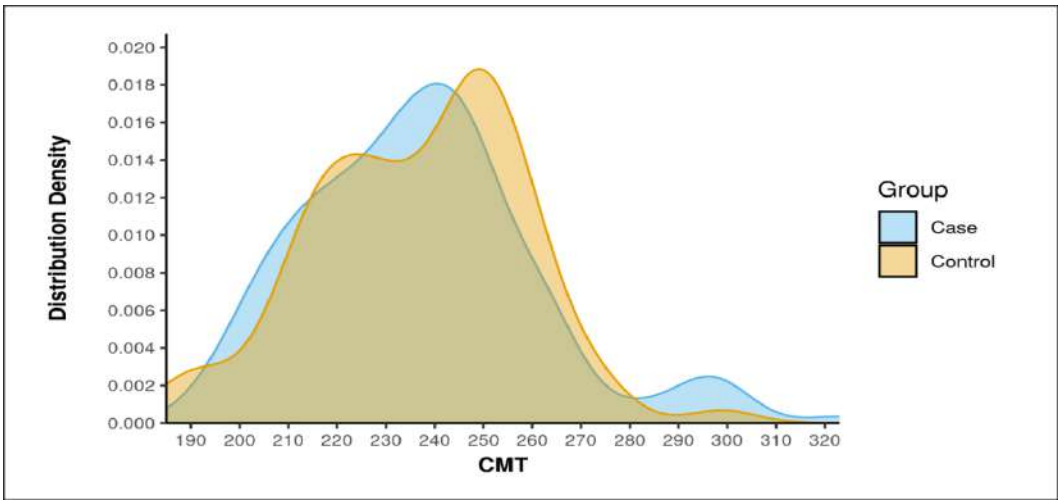

Figure 12 -The density plot depicting the distribution of CMT between cases and controls.

Central macular thickness right eye

The mean of CMT ± SD in right eye in the case and control group was 236.38±23.67 and 237.08 ±21.26µm respectively. The median of CMT in the right eye in the case group was 236 µm with interquartile range of 218-248µm. The median of CMT in right eye in the control group was 241µm with interquartile range of 220-252µm. The CMT in right eye in the case group ranged from 192 - 302µm. The CMT in right eye in the control group ranged from 188 – 299µm.

CMT right eye(µm)	Group		Wilcoxon-Mann-Whitney U Test	
	Case	Control	W	p value
Mean ± SD	236.38 ± 23.67	237.08 ± 21.26	3383.500	0.476
Median (IQR)	236 (218-248)	241 (220-252)		
Min - Max	192 – 302	188 – 299		

Table 12- Comparison of central macular thickness in right eye between cases and controls.

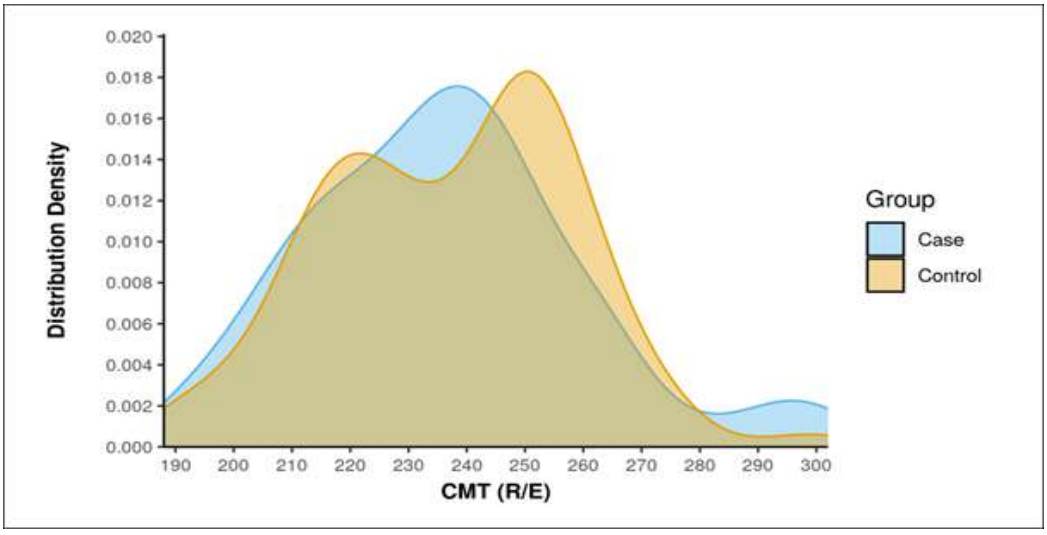

Figure 13 -The density plot depicts the distribution of CMT right eye in the cases and controls

Central macular thickness left eye

The mean ± SD of CMT in left eye in the case and control group was 237.85±24.32 µm and 236.53±21.56µm respectively. The median of CMT in left eye in the case group was 237 µm with interquartile range of 221-250µm. The median of CMT in left eye in the control group was 240 µm with interquartile range of 223-252µm. The CMT in left eye in the case group ranged from 200 - 323µm. The CMT in left eye in the control group ranged from 185 - 299µm.

CMT left eye(µm)	Group		Wilcoxon-Mann-Whitney U Test	
	Case	Control	W	p value
Mean ±SD	237.85 ±24.32	236.53 ±21.56	3516.5	0.766
Median (IQR)	237 (221-250)	240 (223-252)		
Min – Max	200 - 323	185 – 299		

Table 13 - shows the comparison of mean of the central macular thickness left eye between cases and controls

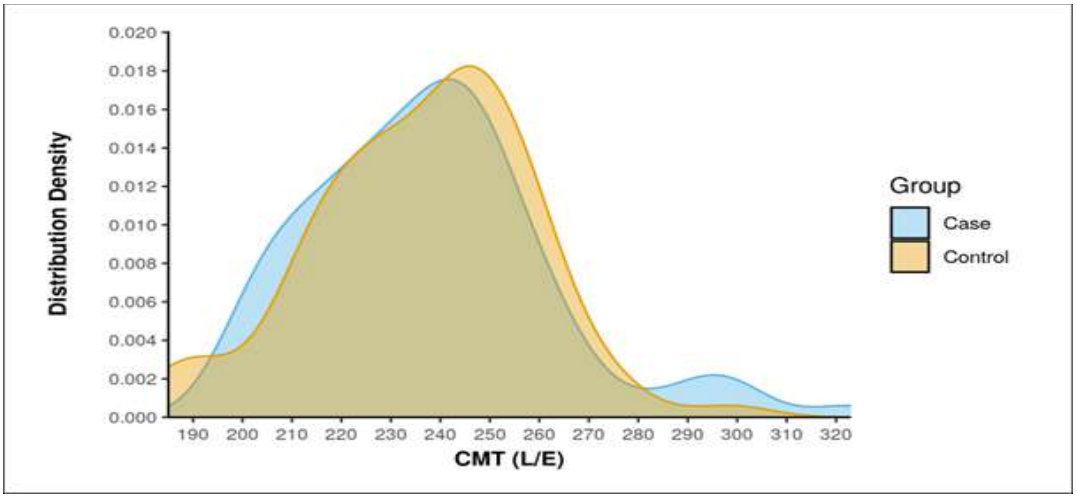

Figure 14 - The density plot depicts the distribution of CMT left eye in cases and controls.

Ganglion layer thickness (GLT)

The mean ± SD of GLT in the case and control group was 84.36 ±5.71 µm and 82.28 ±7.09µm respectively. The median of GLT in the case group was 85 µm with interquartile range of 81-88µm. The median of GLT in the control group was 83µm with interquartile range of 79-86µm. The GLT in the case group ranged from 66 - 97µm. The GLT in the control group ranged from 40-100µm.

There was a significant difference between the 2 groups in terms of GLT (W = 17316.000, p = 0.002), with the median GLT being higher in the case group.

GLT (µm)	Group		Wilcoxon-Mann-Whitney U Test	
	Case	Control	W	p value
Mean ±SD	84.36 ± 5.71	82.28 ± 7.09	17316	0.002
Median (IQR)	85 (81-88)	83 (79-85.75)		
Min – Max	66 - 97	40 – 100		

Table 14-Variation of GLT between cases and controls.

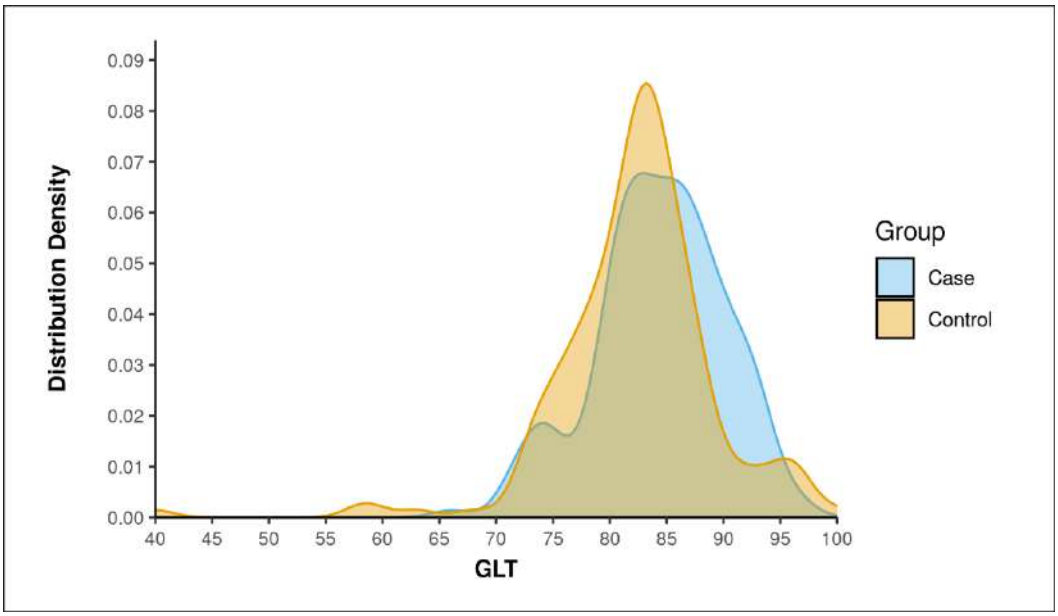

Figure 15 -The density plot below depicts the distribution of GLT in cases and controls.

Ganglion layer thickness right eye (Right eye)

The mean ± SD of GLT in the right eye in the case group was 84.24 ±5.69 µm. The mean of GLT in the right eye in the control group was 82.47 ± 6.03 µm. The median of GLT in the right eye in the case group was 84 µm with an interquartile range of 81-88µm. The median of GLT in the right eye in the control group was 83µm with an interquartile range of 79-86µm. The GLT in the right eye in the case group ranged from 71 - 97µm. The GLT in the right eye in the control group ranged from 58 - 97µm.

GLT right eye(µm)	Group		t-test	
	Case	Control	T	p value
Mean ± SD	84.24 ±5.69	82.47 ±6.03	1.962	0.051
Median (IQR)	84 (81-88)	83 (79-86)		
Min – Max	71 – 97	58 – 97		

Table 15- Comparison of ganglion layer thickness in right eye between cases and controls.

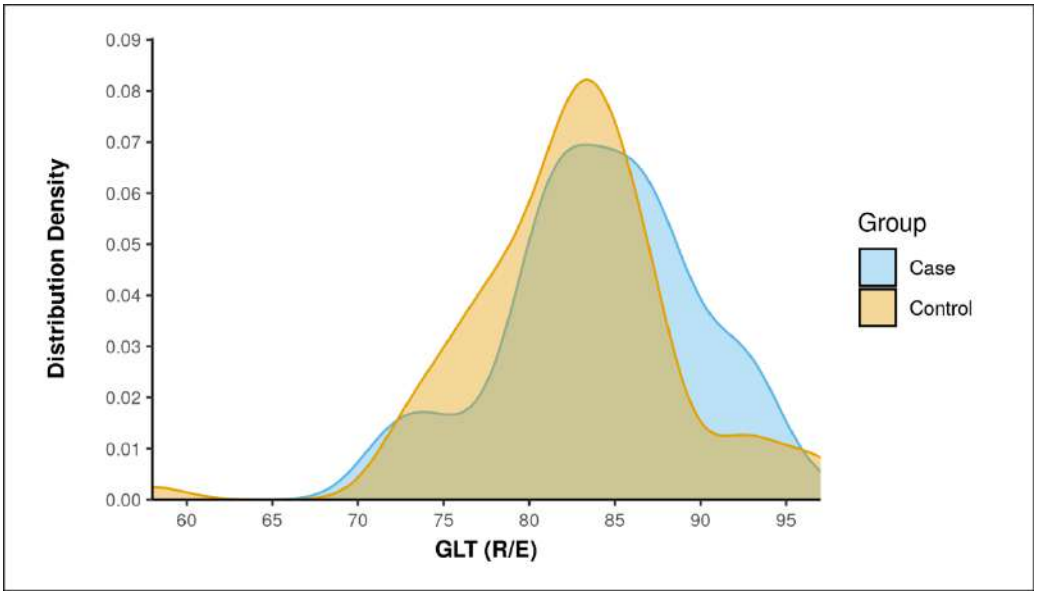

Figure 16 -The density plot depicts the distribution of GLT right eye in cases and controls.

Ganglion layer thickness left eye

The mean ± SD of GLT left eye in the case and control group was 84.48 ±5.77 µm and 82.09 ± 8.04µm respectively. The median of GLT left eye in the case group was 85 µm with an interquartile range of 81-89 µm. The median of GLT left eye in the control group was 83 µm with an interquartile range of 79-85µm. The GLT in the left eye in the case group ranged from 66 - 96µm. The GLT in left eye in the control group ranged from 40 – 100µm.

GLT left eye(µm)	Group		Wilcoxon-Mann-Whitney U Test	
	Case	Control	W	p value
Mean ±SD	84.48 ±5.77	82.09 ±8.04	4372.000	0.018
Median (IQR)	85 (81-89)	83 (79-85)		
Min – Max	66 - 96	40 – 100		

Table 16- Comparison of the means of ganglion layer thickness in the left eye between cases and controls.

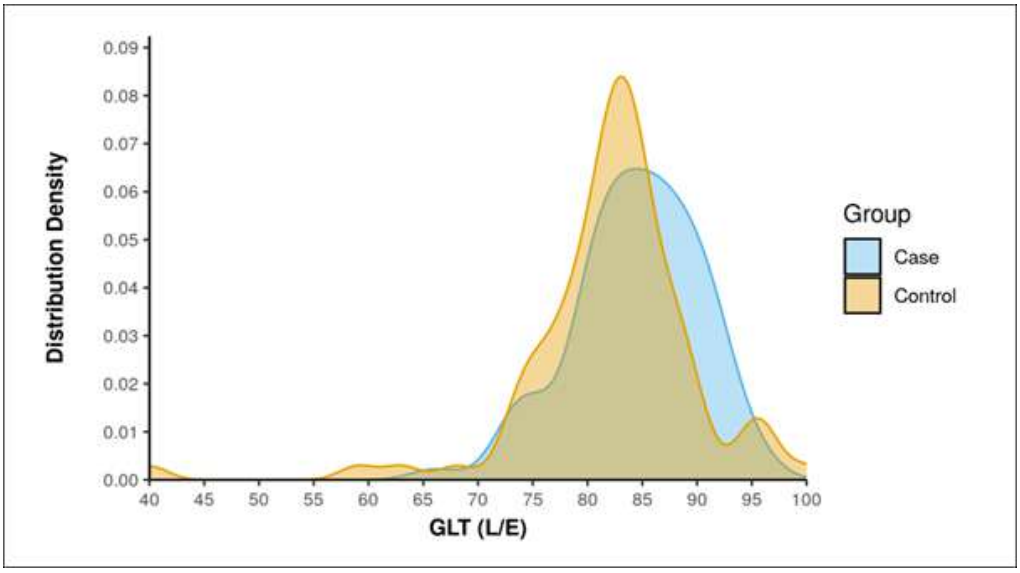

Figure 17 -The density plot depicts the distribution of GLT left eye in cases and controls.

Average RNFL thickness

The mean ± SD of average RNFL thickness in the case group and control group was 96.23 ± 9.32 µm and 93.47 ± 9.68µm respectively. The median of average RNFL thickness in the case group was 96.75 µm with interquartile range of 90.25-103.19µm. The median of average RNFL thickness in the control group was 93.5µm with interquartile range of 86.5-98.94µm. The average RNFL thickness in the case group ranged from 71.75 - 116.25µm. The average RNFL thickness in the control group: ranged from 54.75 - 122.5µm.

There was a no significant difference between the 2 groups in terms of average RNFL thickness (t = 2.681, p = 0.008).

Average RNFL thickness (µm)	Group		t-test	
	Case	Control	t	p value
Mean ± SD	96.23 ± 9.32	93.47 ± 9.68	2.681	0.008
Median (IQR)	96.75(90.25-103.19)	93.5 (86.5-98.94)		
Min – Max	71.75 - 116.25	54.75 - 122.5		

Table 17- The comparison of average RNFL thickness between cases and controls.

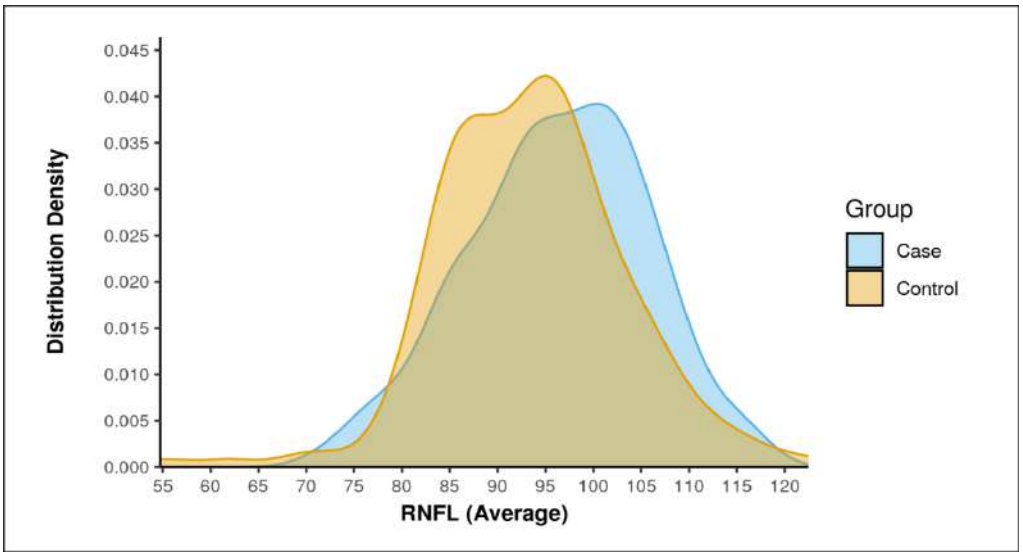

Figure 18 -The density plot depicts the distribution of average RNFL in the cases and controls.

Retinal nerve fibre layer thickness in superior quadrant (RNFL(S)

The mean ± SD of RNFL(S) thickness in the case and control group was 121.32 ±17.70µm and 119.45 ±15.67 µm respectively. The median of RNFL(S) thickness in the case group was 123 µm with interquartile range of 112-133µm. The median of RNFL (S) thickness in the control group was 118 µm with interquartile range of 111-128.75µm. The RNFL(S) thickness in the case group ranged from 77 - 168µm. The RNFL (S) thickness in the control group ranged from 64 - 165µm. There was no significant difference between the groups in terms of RNFL (S) thickness (t = 1.031, p = 0.303).

RNFL(S)(µm)	Group		t-test	
	Case	Control	T	p value
Mean ±SD	121.32± 17.70	119.45± 15.67	1.031	0.303
Median (IQR)	123 (112-133)	118 (111-128.75)		
Min – Max	77 - 168	64 – 165		

Table 18- The comparison of the means of RNFL in superior quadrant between cases and controls.

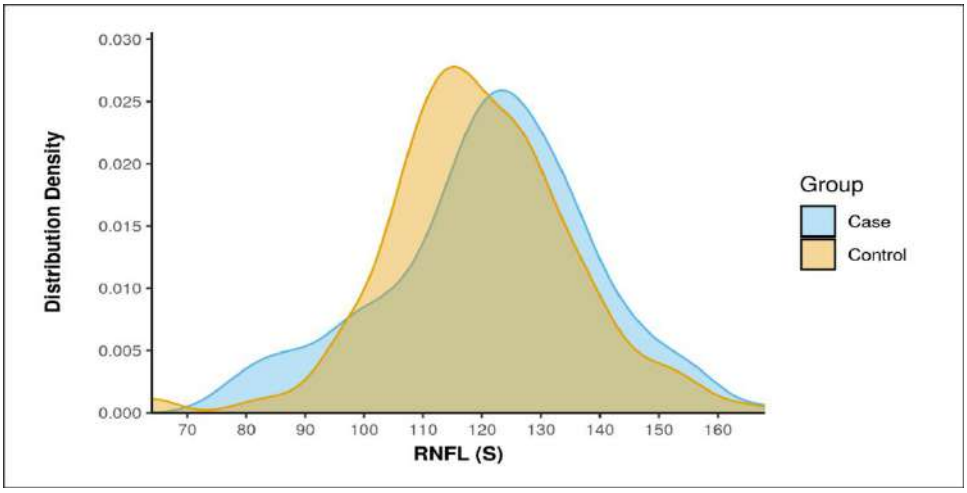

Figure 19 -The density plot depicts the distribution of RNFL (S) thickness in superior quadrant in cases and controls.

Retinal nerve fibre layer thickness in inferior quadrant (RNFL (I)

The mean of RNFL (I) thickness in the case and control group was 127.42 ±15.84 µm and 122.84 ±17.82µm respectively. The median of RNFL(I) thickness in the case group was 128 µm with interquartile range of 116.25-137µm. The median of RNFL (I) thickness in the control group was 121 µm with interquartile range of 114-133µm. The RNFL (I) thickness in the case group ranged from 80 - 175µm. The RNFL (I) thickness in the control group ranged from 53 - 193µm.

There was a no significant difference between the 2 groups in terms of RNFL (I) thickness (t = 2.506, p = 0.013).

RNFL (I)(µm)	Group		t-test	
	Case	Control	T	p value
Mean ± SD	127.42 ± 15.84	122.84 ±17.82	2.506	0.013
Median (IQR)	128 (116.25-137)	121 (114-133)		
Min – Max	80 - 175	53 – 193		

Table 19- The comparison of the means of RNFL in inferior quadrant between cases and controls.

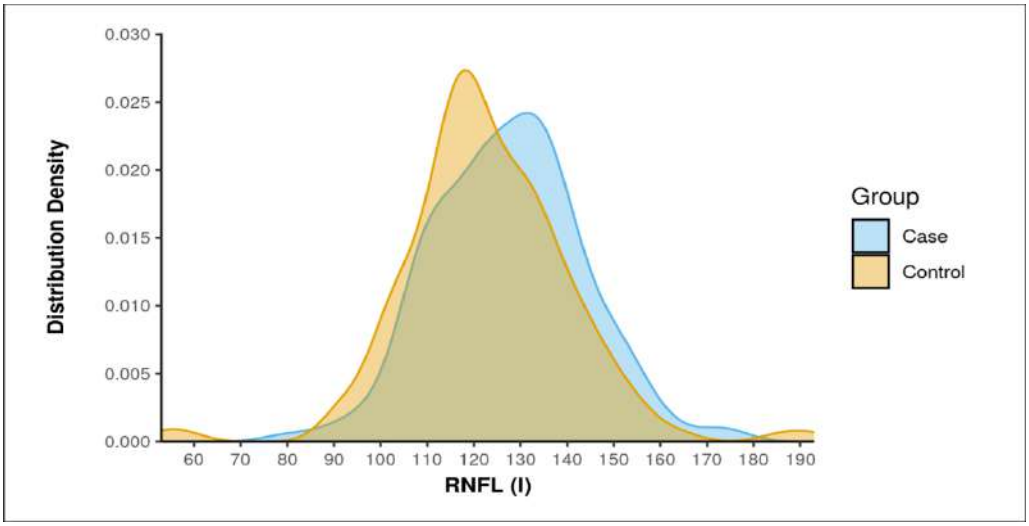

Figure 20 - The density plot depicts the distribution of RNFL in inferior quadrant in cases and controls.

Retinal nerve fibre layer thickness in temporal quadrant (RNFL (T))

The mean ± SD of RNFL (T) thickness in the case and control group was 63.89 ±10.15µm and 61.86 ±9.69µm respectively. The median of RNFL (T) thickness in the case group was 64 µm with interquartile range of 57-71µm. The median of RNFL (T) thickness in the control group was 60 µm with interquartile range of 55-67µm. The RNFL (T) thickness in the case ranged from 36 - 89µm. The RNFL (T) thickness in the control group ranged from 42 - 101µm. There was no significant difference between the 2 groups in terms of RNFL (T) thickness (W = 16629.500, p = 0.016

RNFL (T) (µm)	**Group**		**Wilcoxon-Mann-Whitney U Test**	
	Case	**Control**	**W**	**p value**
Mean ± SD	63.89 ±10.15	61.86 ±9.69	16629.500	0.016
Median (IQR)	64 (57-71)	60 (55-67)		
Min – Max	36 - 89	42 – 101		

Table 20- The comparison of the means of RNFL in temporal quadrant between cases and controls.

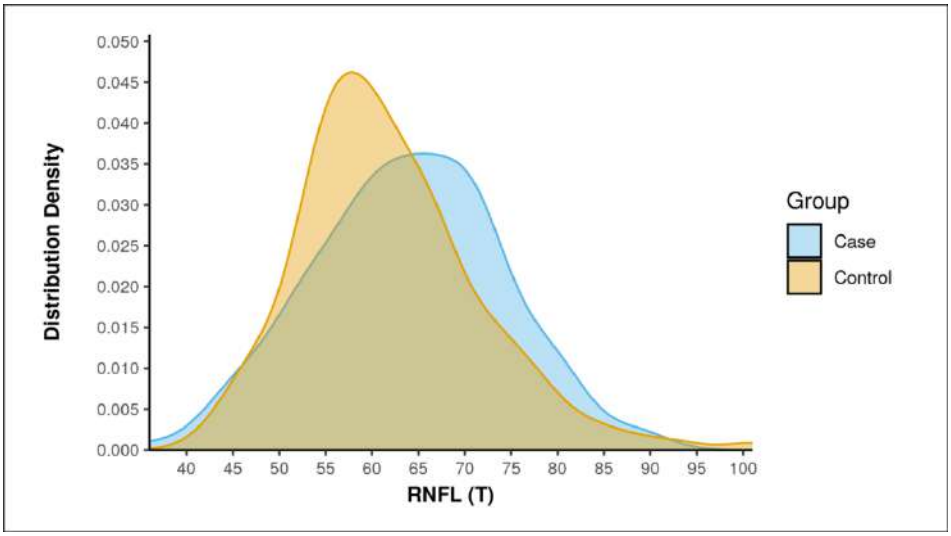

Figure 21 -The density plot depicts the distribution of thickness of RNFL in the temporal quadrant in cases and controls.

Retinal nerve fibre layer thickness in nasal quadrant (RNFL (N))

The mean ± SD of RNFL (N) thickness in the case and control group was 72.31 ±11.97µm. and 69.72 ±10.73µm respectively. The median of RNFL (N) thickness in the case group was 71.5 µm with an interquartile range of 64-81µm. The median of RNFL (N) thickness in the control group was 68 µm with an interquartile range of 62-76µm. The RNFL (N) in the case group ranged from 38 - 103µm. The RNFL (N) in the control group ranged from 49 - 105µm. There was no significant difference between the 2 groups in terms of RNFL (N) µm (W = 16502.500, p = 0.023

RNFL (N) thickness(µm)	**Group**	**Wilcoxon-Mann-Whitney U Test**		
	Case	**Control**	**W**	**p value**
Mean ±SD	72.31 ±11.97	69.72 ±10.73	16502.500	0.023
Median (IQR)	71.5 (64-81)	68 (62-76)		
Min – Max	38 - 103	49 – 105		

Table 21- The comparison of the means of RNFL in nasal quadrant between cases and controls.

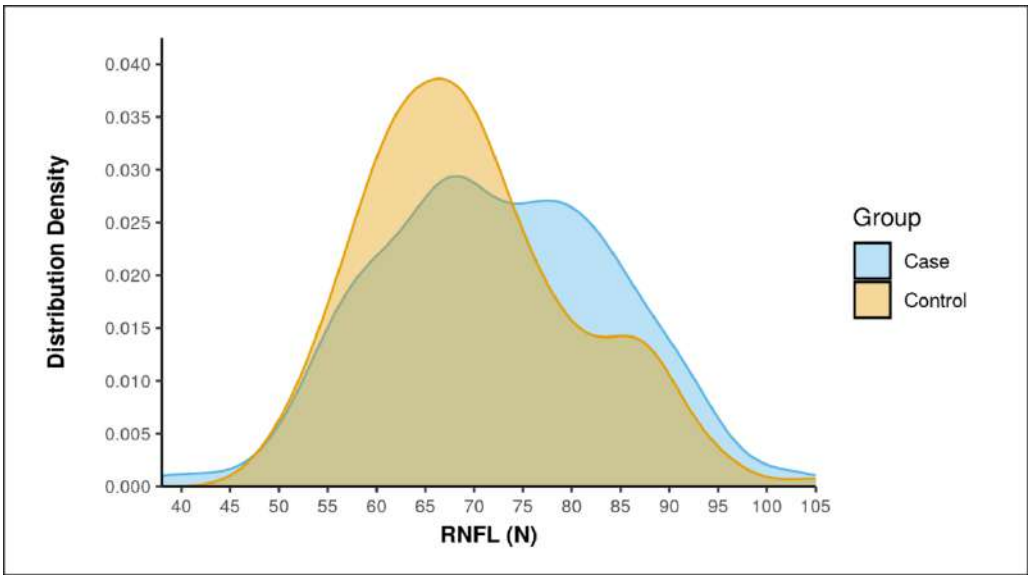

Figure 22 -The density plot depicts the distribution of RNFL in nasal quadrant in cases and controls.

SYSTEMIC PARAMETERS

Systolic BP

The mean ± SD of systolic BP in the case group was 111.65 ±7.38 mm of Hg. The mean of Systolic BP in the control group 110.12 ±10.06 mm of Hg. The median of systolic BP in the case group was 110 mm of Hg with interquartile range of 110-120 mm of Hg. The median of systolic BP in the control group was 110 mm of Hg with interquartile range of 100-120 mm of Hg. The systolic BP in the case group ranged from 100 – 120 mm of Hg. The systolic BP in the control group ranged from 80 – 120 mm of Hg. There was no significant difference between the groups in terms of Systolic BP (mmHg) (W = 3786.000, p = 0.566).

Systolic BP (mmHg)	**Group**		**Wilcoxon-Mann-Whitney U Test**	
	Case	**Control**	**W**	**p value**
Mean ±SD	111.65± 7.38	110.12 ± 10.06	3786	0.566
Median (IQR)	110 (110-120)	110 (100-120)		
Min – Max	100 – 120	80 – 120		

Table 22- Variability of systolic BP between cases and control.

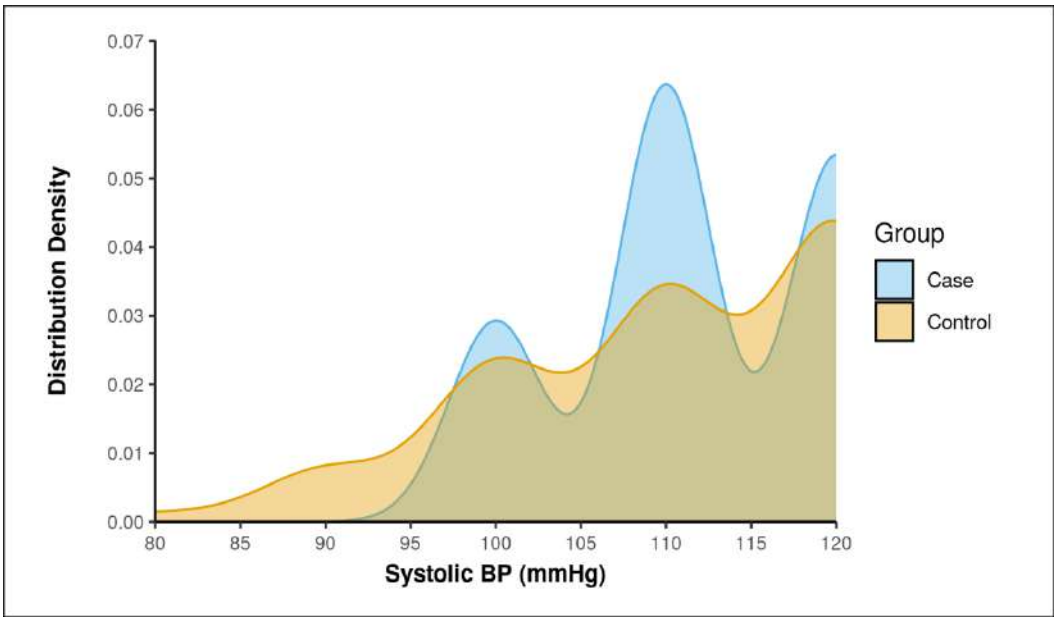

Figure 23-The density plot below depicts the distribution of Systolic BP (mmHg) in the cases and controls.

Diastolic BP

The mean ± SD of diastolic BP in the case group was 77.06 ±8.43 mm of Hg. The mean of diastolic BP in the control group was 76.00 ±7.90 mm of Hg. The median of diastolic BP in the case group was 70 mm of Hg with interquartile range of 70-80 mm of Hg. The median of diastolic BP in the control group was 80 mmHg with interquartile range of 70-80 mm of Hg. The diastolic BP in the case group ranged from 60 – 90 mm of Hg. The diastolic BP in the control group ranged from 60 – 90 mm of Hg. There was no significant difference between the groups in terms of diastolic BP (mmHg) (W = 3735.500, p = 0.682).

Diastolic BP (mmHg)	**Group**		**Wilcoxon-Mann-Whitney U Test**	
	Case	**Control**	**W**	**p value**
Mean ±SD	77.06 ±8.43	76.00 ±7.90	3735.500	0.682
Median (IQR)	70 (70-80)	80 (70-80)		
Min – Max	60 – 90	60 – 90		

Table 23 - Variability of diastolic BP between cases and controls.

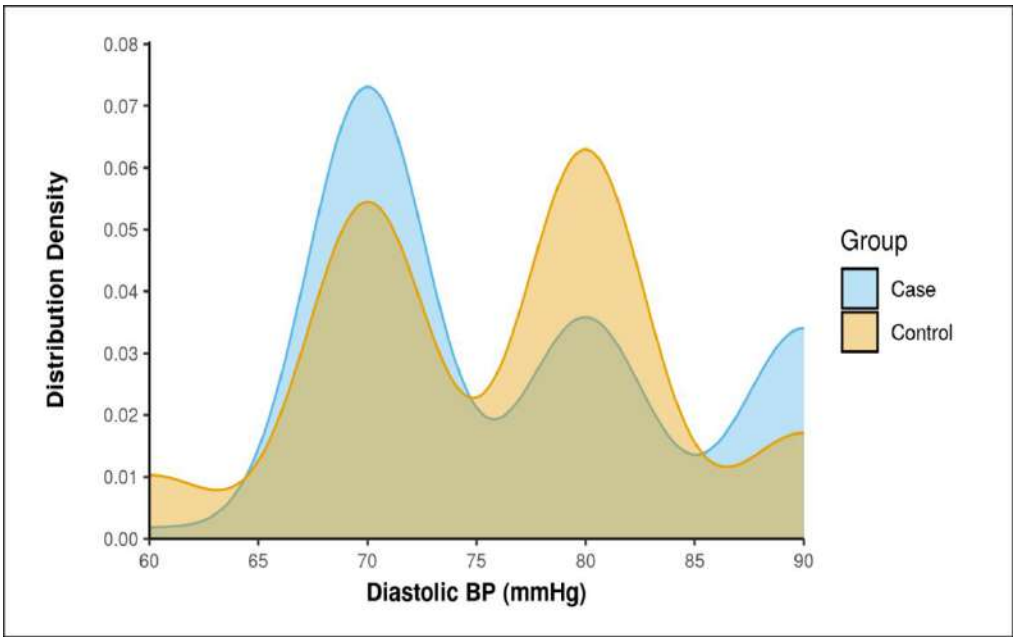

Figure 24 -The density plot depicts the distribution of diastolic BP (mmHg) in the cases and controls.

Respiratory rate (RR)

The mean ± SD of RR in the case group was 24.76 ±1.34 per minute. The mean of RR in the control group was 22.02 ±1.77 per minute. The median of RR in the case group was 24 per minute with interquartile range of 24-25 per minute. The median of RR in the control group was 21 per minute with interquartile range of 21-24 per minute. The RR in the study group ranged from 23 – 31 per minute. The RR in the control group ranged from 20– 26 per minute. There was a significant difference between the 2 groups in terms of RR (CPM) (W = 6334.000, p = <0.001), with the median RR being higher in the case group.

RR (CPM)	Group		Wilcoxon-Mann-Whitney U Test	
	Case	Control	W	p value
Mean ±SD	24.76 ±1.34	22.02 ±1.77	6334.00	<0.001
Median (IQR)	24 (24-25)	21 (21-24)		
Min – Max	23 – 31	20 – 26		

Table 24 - Variability of respiratory rate among cases and controls

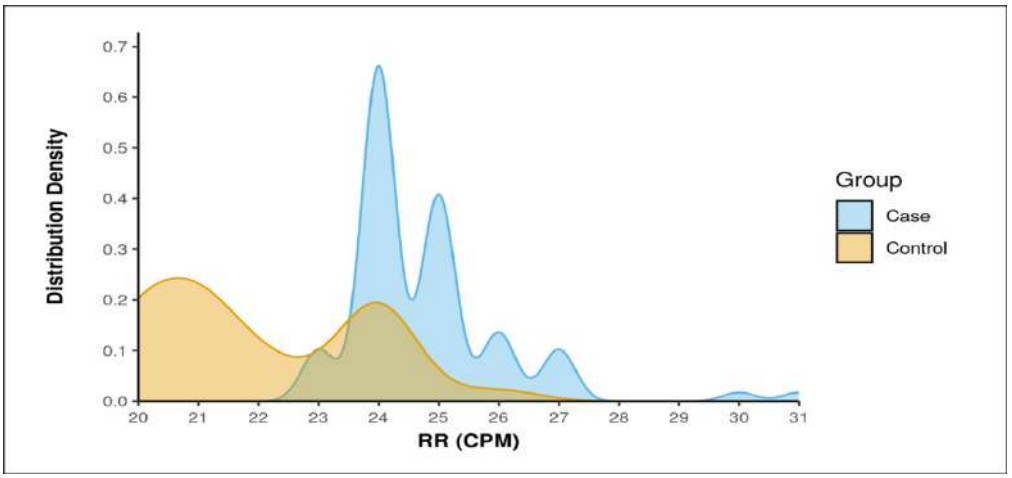

Figure 25-The density plot depicts the distribution of RR in cases and controls.

Oxygen saturation

The mean ± SD of SpO2 in the case and control group was 97.99 ±0.73% and 98.12 ±0.82%, respectively. The median of SpO2 in the case group was 98% with an interquartile range of 97-99%. The median of SpO2 in the control group was 98% with an interquartile range of 97-99%. The SpO2 in the case group ranged from 97 – 99 %while the SpO2 in the control group ranged from 96 – 99%. There was no significant difference between the groups in the terms of SpO2% (W = 3251.500, p = 0.231).

SpO2 (%)	Group		Wilcoxon-Mann-Whitney U Test	
	Case	Control	W	p value
Mean ±SD	97.99 ±0.73	98.12 ±0.82	3251.500	0.231
Median (IQR)	98 (97-99)	98 (97-99)		
Min - Max	97 – 99	96 – 99		

Table 25- Variability of oxygen saturation among cases and controls.

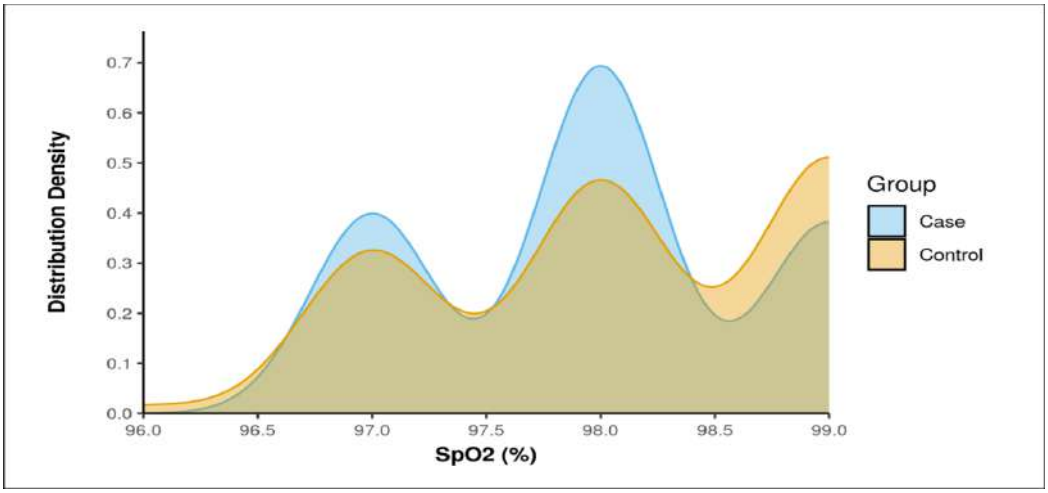

Figure 26 - The density plot depicts the distribution of SpO2 (%) in the cases and controls.

Heart rate

The mean ± SD of heart rate in the case group was 85.86 ±8.46 per minute. The mean of heart rate in the control group was 84.22 ±0.76 per minute. The median of heart rate in the case group was 85 per minute with interquartile range of 84-87 per minute. The median of heart rate in the control group was 84 per minute with interquartile range of 84-85 per minute. The heart rate in the case group ranged from 25 – 110 per minute. The heart rate in the control group ranged from 83 – 85 per minute. There was a significant difference between the 2 groups in terms of heart rate (W = 4830.500, p = <0.001), with the median heart rate being higher in the case group.

Heart Rate	**Group**		**Wilcoxon-Mann-Whitney U Test**	
	Case	**Control**	**W**	**p value**
Mean ±SD	85.86 ±8.46	84.22 ±0.76	4830.500	<0.001
Median (IQR)	85 (84-87)	84 (84-85)		
Min – Max	25 – 110	83 – 85		

Table 26 - Variability of heart rate among cases and controls

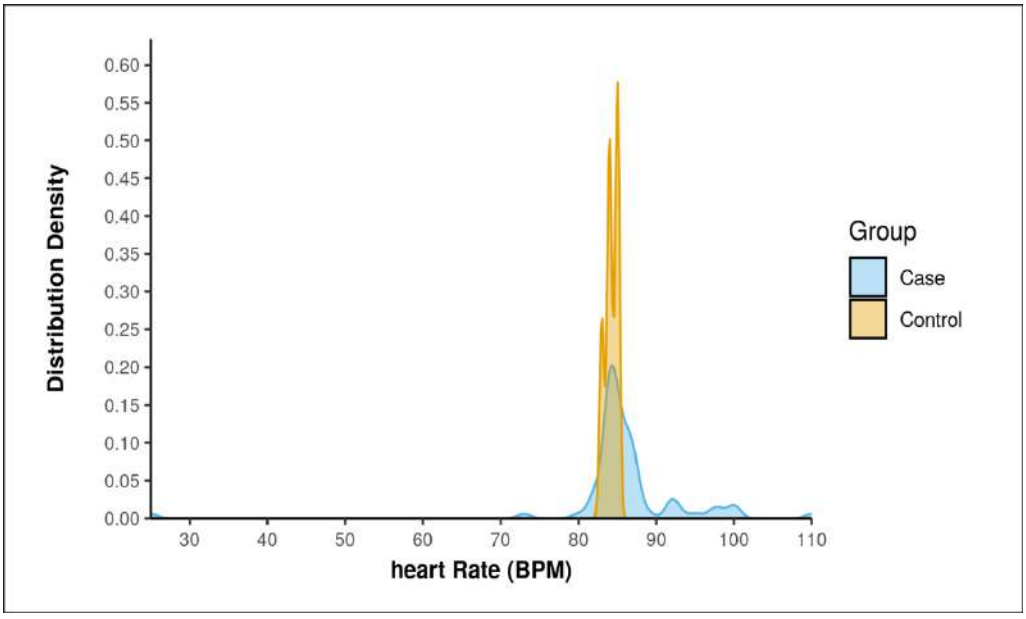

Figure 27 - The density plot depicts the distribution of heart rate in the cases and controls.

Co morbid endocrine disorders

In the study group, 64 patients had a history of associated comorbid endocrine disorders of which 8 patients had a history of diabetes. 60 patients had a history of hypothyroidism; 2 males had a history of hypoparathyroidism while 12 patients had a history of delayed puberty.

Co-existent endocrine disorders	Males	Females	Total
Diabetes	6	2	8
Hypothyroidism	36	24	60
Hyperparathyroidism	2	0	2
Delayed Puberty	6	6	12

Table 27 - Distribution of endocrine disorders in cases

Transfusion transmitted infection

6 males and 6 females had a history of hepatitis C. None of the patients had hepatitis B or HIV.

Type of chelation

Among the cases, 47 (55.29%) patients were on combination chelation therapy consisting of deferiprone+deferasirox,6 (7.06%) were receiving deferoxamine + deferasirox,1 (1.18%) was on deferoxamine +deferiprone and 31 (36.47%) were on only deferasirox therapy.

Type Of Chelation	Number(n=85)	Percentage (%)
Deferiprone+Deferasirox	47	55.29
Deferasirox	31	36.47
Desferoxamine+Deferasirox	6	7.06
Desferoxamine+Deferiprone	1	1.18

Table 28-Various chelation therapies thalassemia patients were undergoing

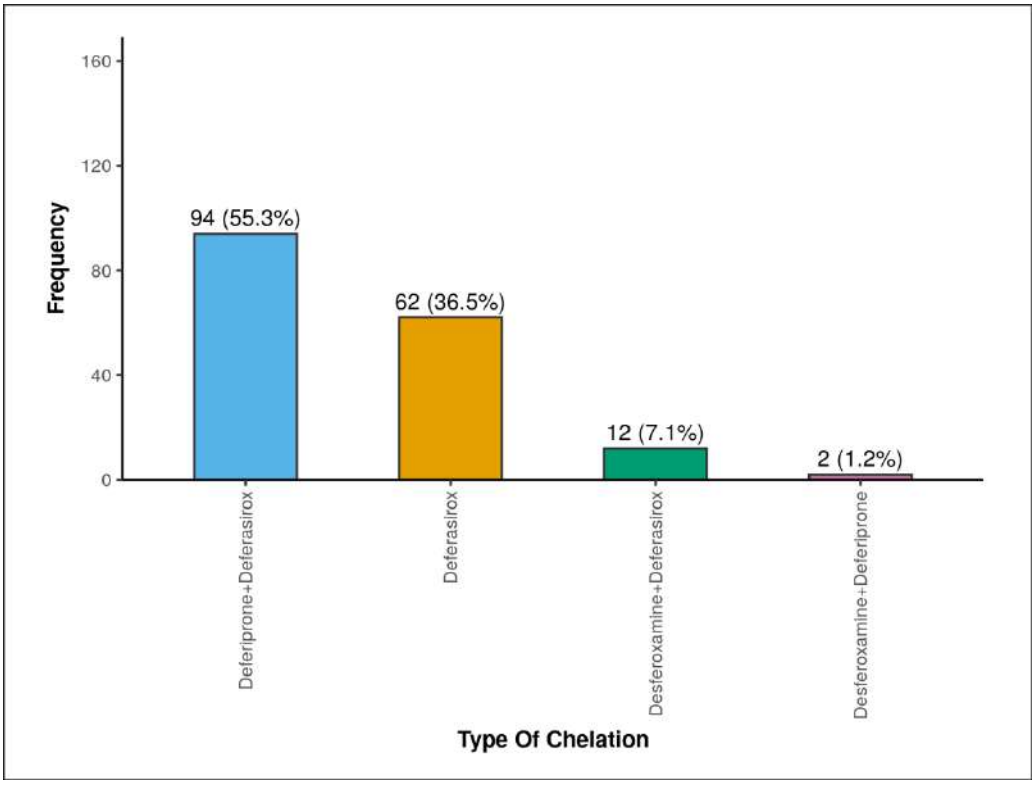

Figure 28 - Various chelation therapies the thalassemia patients were undergoing, during the study period.

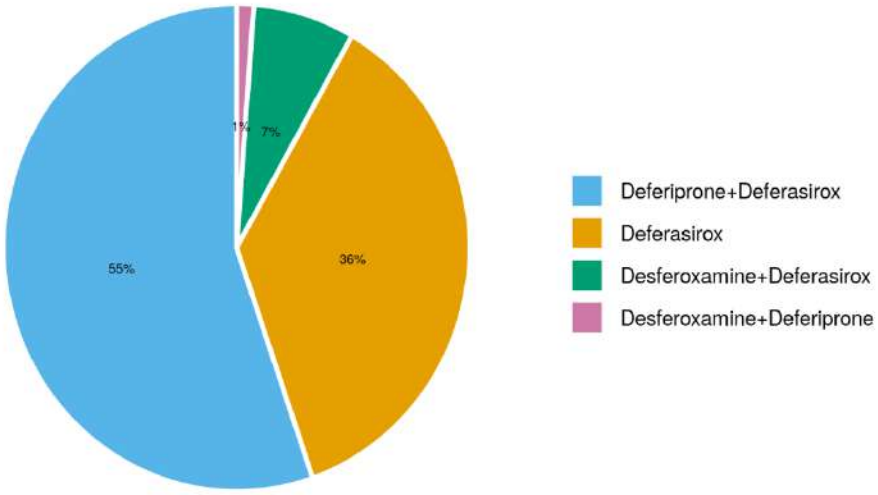

Figure 29 - Distribution of cases on the basis of chelation therapy

Duration of chelation

The mean ± SD of the duration of chelationin the case group was 11.95±5.60years. The median duration of chelation in the male group was 14 years with an interquartile range of 8-15years. The duration of chelation in the patients ranged from 0.5 – 22years.

Duration Of Chelation (Years)	
Mean ±SD	11.95 ±5.60
Median (IQR)	14 (8-15)
Range	0.5– 22

Table 29-Duration of chelation in thalassemia patients.

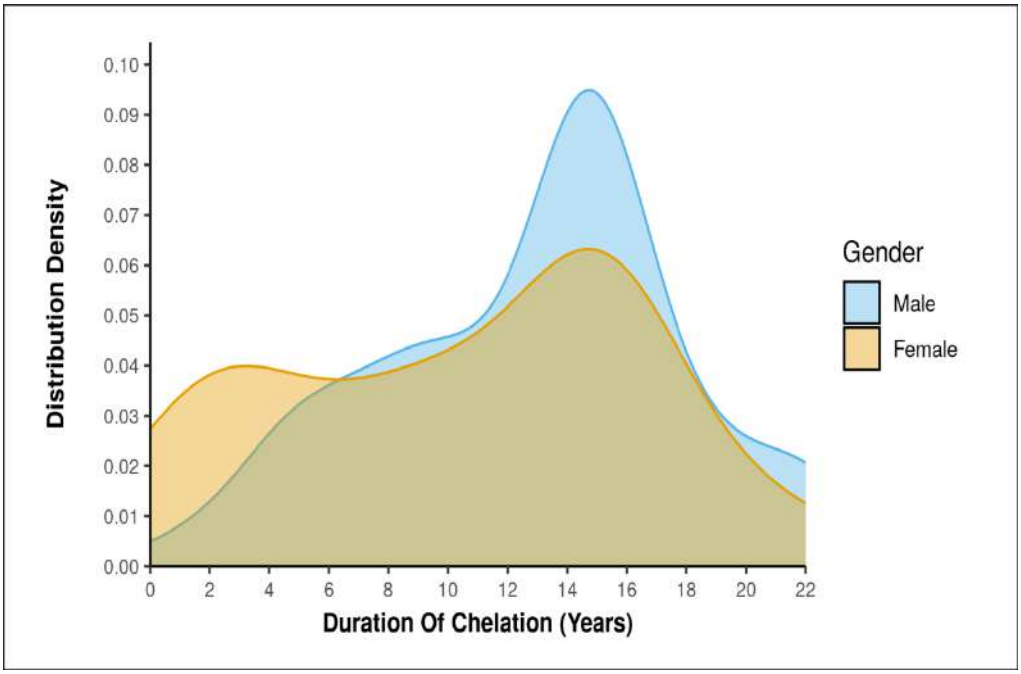

Figure 30 -The density plot depicts the distribution of duration of chelation in years.

Average haemoglobin over 5 years

In the study group, the mean ±SD of average Hb over 5 years was 9.13 ±0.47g/dl. The median of average Hb over 5 Years in the patients was 9.2 g/dL with an interquartile range of 8.9-9.4 g/dl. The patients' average Hb over 5 Years ranged from 7.9 - 11.4 g/dl.

Average Haemoglobin Over 5 Years (g/dL)	
Mean ± SD	9.13 ± 0.47
Median (IQR)	9.2 (8.9-9.4)
Range	7.9 - 11.4

Table 30 - Average haemoglobin over 5 years in the case group

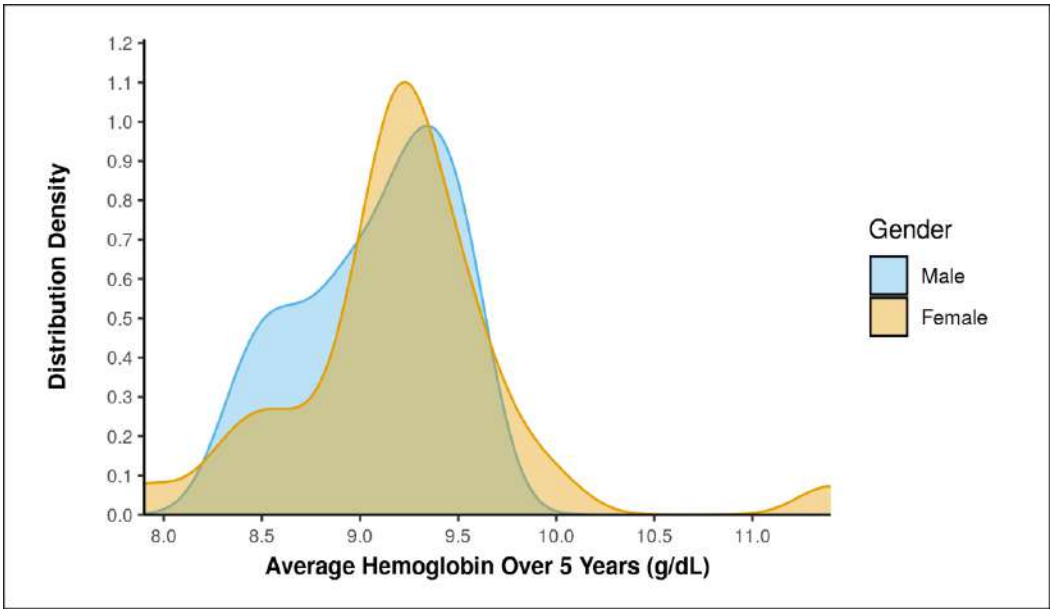

Figure 31 -The density plot depicts the distribution of average hemoglobin over 5 Years (g/dL) in the cases.

Average transfusion requirement

Among the cases, the mean ± SD of average transfusion requirement over 5 years was 212.08±57.03 ml/kg/year. The median average transfusion requirement over 5 years in the patients was 225ml/kg/year. The average transfusion requirement over 5 years in the patients ranged from 92–431 ml/kg/year.

Average Transfusion Requirement Over 5 Years (ml/kg/year)	
Mean ±SD	212.08±57.03
Median	225
Range	92-431

Table 31 - The average transfusion requirement (ml/kg/year) in cases.

Serum ferritin levels

Among the cases, the mean ± SD of serum ferritin levels was 2607.27±1931.28 ng/ml. The median of serum ferritin levels in the patients was 2146 ng/ml with an interquartile range of 1288-3593ng/ml. The serum ferritin levels in the patients ranged from 207 – 14177ng/ml.

Serum Ferritin Levels	
Mean ± SD	2607.27 ± 1936.98
Median (IQR)	2146 (1288-3593)
Range	207 – 14177

Table 32- Serum ferritin levels in the study subjects.

Serum ferritin levels(ng/ml)	**Number of patients (n=85)**	**Percentage of patients (%)**
<1000	13	15.29
1000-2500	36	42.36
2500-5000	30	35.29
>5000	6	7.06

Table 33- Distribution of the patients based on serum ferritin levels (ng/ml)

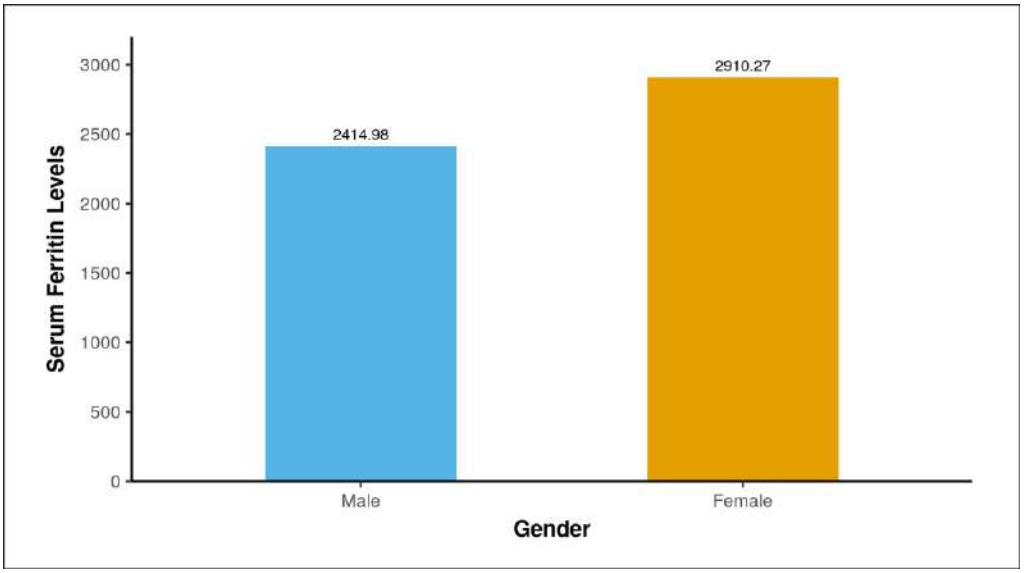

Figure 32 -The bar graph depicts the means of serum ferritin levels in the cases.

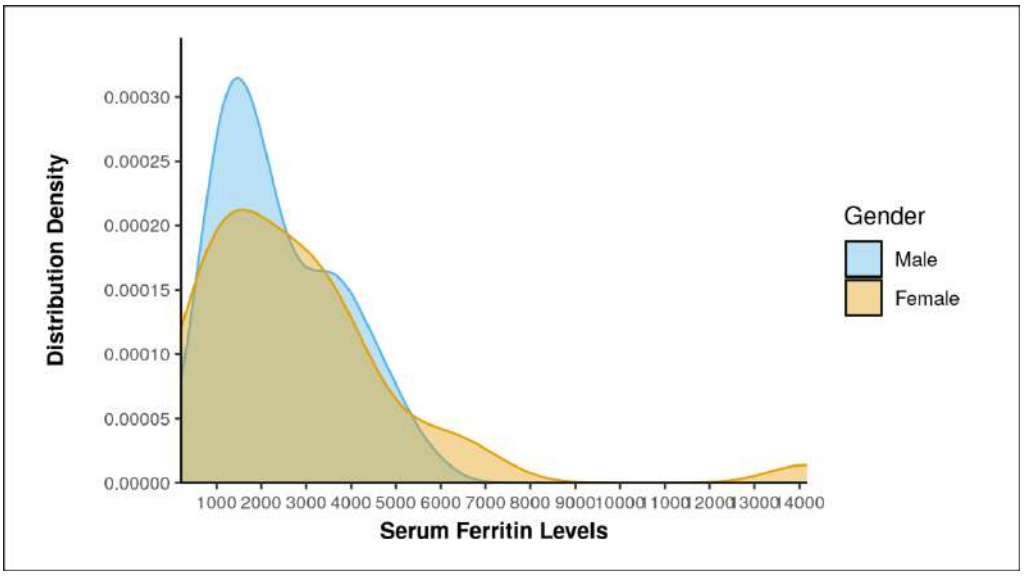

Figure 33 -The density plot depicts the distribution of serum ferritin levels in the cases.

Liver iron concentration (LIC)

Among the cases, the mean of LIC was 11.84±12.02 mg/g dry weight of liver. The median of LIC in the patients was 8.36 mg/g with an interquartile range of 3.51-17.28mg/g dry weight of liver. The LIC in the patients ranged from 0.72 - 49.5 mg/g dry weight of liver.

LIC (mg/g dry weight of liver)	
Mean ± SD	11.84 ±10.60
Median (IQR)	8.36 (3.51-17.28)
Range	0.72 - 49.5

Table 34-Liver iron concentration in various study subjects

Liver iron concentration (mg/g dry weight of liver)	**Number of patients (n=85)**	**Percentage of patients (%)**
Normal	8	9.41
Mild	16	18.82
Moderate	13	15.29
Severe	19	22.36
Not Attempted	29	34.12

Table 35- Distribution of patients based on LIC levels.

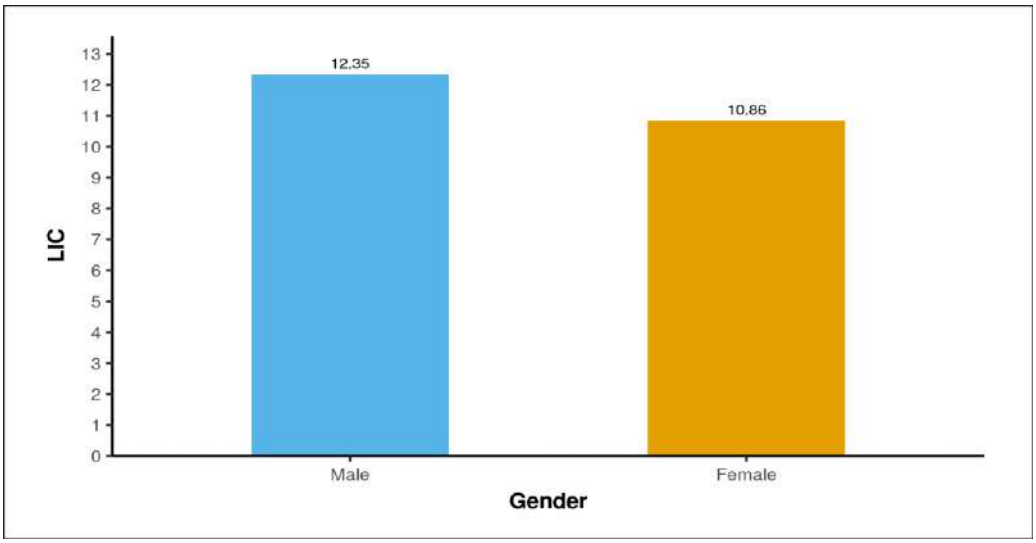

Figure 34 -The bar graph depicts the means of LIC in the cases.

Cardiac MRI

Among the cases, the mean myocardial iron concentration (MIC) was 1.83±3.40 mg/g dry weight of myocardium. The median MIC in the patients was 0.68 mg/g/dry weight of myocardium. MIC in the patients ranged from 0.29–22 mg/g weight of myocardium.

Myocardial iron concentration (mg/g weight of myocardium)	
Mean ±SD	1.83±3.40
Median	0.68
Range	0.29–22

Table 36- The myocardial iron concentration (mg/g dry weight of myocardium) on cardiac MRI in cases.

Myocardial iron concentration (mg/g dry weight of myocardium)	**Number of patients**	**Percentage (%)**
Normal	44	51.76
Mild	3	3.53
Moderate	3	3.53
Severe	7	8.24
Not Attempted	28	32.94

Table 37- Distribution of patients based on myocardial iron concentration (MIC).

DISCUSSION

Thalassemia has been identified by the World Health Organization (WHO) as a significant global health concern and is included in the current global burden of disease study. In the Indian subcontinent, the prevalence of genetic Hb disorders is 1.2 per 1,000 live births, with 16,700 births per year affected by thalassemia and sickle cell anaemia. The average frequency of β-thalassemia carriers in India ranges from 3% to 10%.[46] Thalassemia patients' survival rates and overall quality of life have been greatly influenced by two major treatment advancements: regular blood transfusions and iron chelation therapy. The epidemiology of TDT has evolved through the combined efforts of healthcare professionals, increased awareness among families, and government initiatives.

Patients with TDT exhibit a wide range of ocular and systemic symptoms. These include reduced visual acuity, colour vision abnormalities, night blindness, visual field defects, cataracts, retinopathy, and optic neuropathy. While iron-chelating medications like DFO and DFP are implicated in some ocular changes, many are primarily associated with the progression and severity of the disease itself. Current treatment for TDT focuses on reducing serum iron and ferritin levels through iron-chelating agents. Regular ophthalmic examinations are thus essential for preventing or managing ocular complications effectively, thereby mitigating the impact of severe ocular issues.[12,47]

Selecting an appropriate method to assess and monitor fundus changes in TDT is crucial for investigating the effectiveness and safety of iron chelators. As imaging devices advance, there's a transition from standard fundus photographs to more detailed, microscopic, and three-dimensional imaging of retinal layers. This shift promises increased precision and personalized monitoring of lesions and changes in the future. Additionally, the integration of image stabilization technologies is expected to enhance the reproducibility of structural measurements, helping to distinguish true progression from variability.[12]

Imaging technologies such as OCT, OCT-A,Fundus autofluorescence (FAF), and confocal scanning laser ophthalmoscopy can offer precise estimation and close monitoring of fundus changes, making them valuable additions in trials evaluating iron chelator efficacy and safety.[12]

In the current study, we found that the mean age of the case group was 18.29 ± 6.86 years, while the control group had a mean age of 20.87 ± 3.24 years. The case group consisted of 61.2% males and 38.8% females, whereas the control group had 42.4% males and 57.6% females. However, Uzun et al.[35], in his study included slightly younger study subjects, where the mean ages of the cases and controls were 13.7 ± 2.1 and 14.3 ± 2.2 years, respectively.

Aksoy et al.[29] in his study compared RNFL thickness between three cohorts: TDT patients(mean age -9.65 ± 4.13 years), iron deficiency anaemia patients (mean age - 9.14 ± 2.53 years), and controls (mean age - 9.13 ± 3.29 years). Haghpanah et al.[39] conducted a study in older study subjects(mean age of cases and controls- 28.6 ± 6.2 years and27.1 ± 6.0 years respectively).

In our study, the mean age at diagnosis for TDT patients in males was 20.71 ± 45.77 months while that in females was 28.09 ± 33.31 months. A study by Trehan et al.[27] reported a mean age at presentation of 17.2 ± 19.9 months. In 1975, Kattamis et al[48] observed the age at presentation to be 13.1 months (ranging from 2 to 36 months). Cao [1] reported the mean age of children presenting with TM to be 8.4 ± 9.1 months. In 1984, Modell and Berdukas[28] noted that 60% of patients presented within the first year of life, with a mean age of 6 months. The earlier age of diagnosis in males is attributed to the female disadvantage prevalent in many parts of the country, especially in the northern states. Studies across India have consistently found that boys are more likely than girls to be taken to a health facility when ill.[49]

The mean age at which transfusion was initiated in our cohort was 19.89 ± 24.68 months and the average haemoglobin level was 9.13 ± 0.47 g/dl. Patients with TDT require regular lifelong blood transfusion therapy, which is usually started before 2 years of age.[50] If blood

transfusion is not initiated in time, these children die within first or second decade of life.

Serum ferritin, LIC,and MIC canbe used as a widely available tool for evaluating iron overload. Serum ferritin levels serve as a clinical indicator for directing chelation therapy. The mean serum ferritin levels in our cohort was 2607.27±1931.28 ng/dl, the mean LIC was 11.84±12.02 mg/g dry weight of liver and the mean myocardial iron concentration was 1.84 ± 3.41 mg/g dry weight on T2- weighted MRI.[51]

Various studies have tried to correlate various ocular findings with a number of transfusions, serum ferritin, and serum Hb levels. Taneja et al.[17] observed a significant correlation between lenticular opacities and both serum ferritin levels and the number of blood transfusions patients required. Additionally, they reported a higher incidence of RPE degeneration, RPE mottling, and changes in visual acuity in patients with elevated serum iron and ferritin levels and those needing more transfusions. Barteselli et al.[21] found a greater occurrence of fundus abnormalities, such as PXE, angioid streaks, and CNV, in patients who had undergone splenectomy and were receiving transfusion and chelation therapy. Consequently, frequent monitoring of serum ferritin levels and maintaining the deferoxamine therapeutic index (daily dose per body weight in mg/kg divided by serum ferritin level in mg/l) below 0.025.[52] may help prevent the development of rapidly progressing, severe, and irreversible retinopathy.

In this study, 95.3% of patients had a BCVA of 6/6, while four patients had a BCVA of less than 6/6 due to cortical cataracts. All control group participants had a BCVA of 6/6, resulting in a significant difference in BCVA distribution between the two groups ($p = 0.007$). This finding contrasts with studies by Basiony et al [38] and Haghpanah et al.[39], which reported no significant differences in refractive errors between their case and control groups.

Among the patients with cortical cataracts, four patients (eight eyes) were affected. Three of these patients (6.3%) were on a combination of chelation therapy with DFP and DFX, while one patient (3.2%) was on DFX alone. Although DFO is commonly associated with increased ocular side effects, recent studies have also reported cataracts in patients using DFP. Mehdizadeh et al.[20] and Parakh et al.[19] observed a higher incidence of cataracts in patients undergoing DFP chelation therapy.

It is suggested that the small size and water-solubility of DFP allow it to penetrate cell membranes, including the blood-ocular barrier, leading to its accumulation in the aqueous humour. This accumulation can inhibit the enzyme glutathione peroxidase, resulting in lenticular opacities. Additionally, transient shifts in iron caused by DFP might lead to iron deposition in various organs, including the lens, resulting in subcapsular opacities.[19,20]

There was no significant difference in IOP between the groups ($p = 0.097$). This finding aligns with the study by Uzun et al.[35], which reported mean IOP values of 13.2 (range 9-19) mm Hg in thalassemia patients and 12.8 (range 10-18) mm Hg in controls, with no significant difference between the groups. Similarly, Basiony et al.[38] found mean IOP values of 13.2 ± 0.37 mm Hg in the thalassemia group and 11.93 ± 0.42 mm Hg in the control group, also with no significant difference. Haghpanah et al.[39] reported a mean IOP of 15.51 ± 3.25 mm Hg in thalassemia patients, with only one patient having an IOP of 24 mm Hg. In contrast, Jafari et al.[45] observed a statistically significant increase in IOP in thalassemia patients compared to controls, potentially due to iron overload in the trabecular meshwork.

Schirmer and TBUT tests were conducted as part of the routine ocular examination. The median of TBUT in cases was 5 while in controls was 8.5. There was a significant difference between the 2 groups in terms of TBUT ($p = <0.001$), with the median TBUT being lowest in cases.

The median of Schirmer values in cases was 8 while that in controls was 15. There was a significant difference between the 2 groups in

terms of Schirmer (p = <0.001), with the median Schirmer being lower in the case group.

These findings are consistent with the study by Gartaganis et al.[14], which also reported significantly lower TBUT and Schirmer values in thalassemia patients. Additionally, Gartaganis et al. performed rose Bengal staining and conjunctival cytology, suggesting that squamous metaplasia of the conjunctival epithelium, evidenced by goblet cell loss, could be responsible for the dry eye observed in thalassemia patients.

In our study, the mean CMT for the case group was 237.11 ± 23.94 µm, and for the control group, it was 236.81 ± 21.35 µm. There was no significant difference between cases and controls.

Haghpanah et al.[39] reported significant foveal thinning in TM patients compared to controls. Similarly, El-Shazly et al.[53] found significant foveal thinning in TM patients, particularly those on DFO rather than DFX. Haghpanah [39], however, did not find a correlation between chelation therapy and foveal thinning but did observe a significant negative correlation between haemoglobin levels and CMT, attributing the foveal thinning to anaemia. Conversely, studies by Ulusoy et al.[36] and Baryamoglu et al.[40] did not find significant differences in CMT between cases and controls.

The mean Ganglion Cell Layer Thickness (GLT) in the case group was 84.36 ± 5.71 µm, compared to 82.28 ± 7.09 µm in the control group. A significant difference was observed between the two groups regarding GLT (p = 0.002), with the median GLT being higher in the case group.

Only a few studies have evaluated GLT in TM patients. Ulusoy et al.[36] reported reduced GLT in TM patients, though it was not significant, attributing the thinning to the ischemic potential.

Thus, GLT needs to be investigated and studied further in view of variability of results in the few studies that are conducted.

The mean of average RNFL in the case group was 96.23 ± 9.32 µm while the mean of average RNFL in the control group was 93.47 ± 9.68µm with no significant difference between two groups. (p=0.008).

Likewise, Bayramoglu et al.[40], in his study reported no significant difference in mean RNFL thickness between cases and controls. Haghpanah et al.[39] also showed no significant difference between cases and controls in terms of RNFL. Similarly Ulusoy et al.[36] reported no significant difference between cases and controls in their study. Similar results have been reported by in thalassemia minor patients.[54,55]

However, Uzun et al.[35], demonstrated decreased average RNFL thickness, right nasal, right inferior and right and left temporal RNFL thicknesses. Likewise, Aksoy et al.[29], reported RNFL thinning in all quadrants in TM patients. Datta et al.[37], reported significant thinning in all quadrants in TM patients with nasal quadrant being thinnest followed by temporal, inferior and superior quadrants. Basiony et al.[38] reported significant thinning of RNFL in TM patients in nasal, nasal superior and nasal inferior quadrant. He also reported thinning in left temporal superior quadrant in TM patients as compared to controls.

In the current study, the average RNFL was not having any statistically significant correlation with systemic parameters like serum haemoglobin, serum ferritin levels, average transfusion requirement, duration of chelation, LIC and MIC. Haghpanah et al.[39], found no correlation with age, ferritin or haemoglobin levels. Superior RNFL however had a significant negative correlation with serum ferritin levels in this study.

Ulusoy et al.[36], Uzun et al.[35] and Acer et al.[54], found no correlation between RNFL thickness and parameters like ferritin and haemoglobin. Basiony et al.[38] reported no significant correlation of average RNFL thickness with serum ferritin, serum Hb however, the nasal superior sector was significantly correlated with serum Hb and the temporal superior and nasal sectors were significantly correlated with serum ferritin. Inferior temporal quadrant was significantly correlated with age in this study.

Aksoy et al.[29], reported a negative correlation of RNFL thickness and serum ferritin levels but a positive correlation with Hb levels. Similarly,

Datta et al.[37] also demonstrated a positive correlation of Hb levels with RNFL thickness.

Study	Clinical profile	Number of subjects	Mean age (years)	Number of males	Number of females	Hb (g/dl)	Ferritin(ng/ml)	IOP(mm of Hg)
Aksoy et al	TDT	47	9.65±4.13	17	30	6.574±0.77	2514.40±1791.34	14.5106±1.92
	IDA	22	9.14±2.53	8	14	7.364±1.62	6.50±2.48	13.6842±1.33
	Healthy controls	59	9.13±3.29	32	24	14.864±0.99	17.37±2.23	14.4068±1.49
Uzun et al	TDT	47	13.7±2.1	21	26	8.7 ± 0.45 (gr/dl).	1800 (1450)	12.8
	Controls	51	14.3±2.2	20	51	N/A	N/A	13.2
Ulusoy et al	TDT	32	24.45	14	18	9.77±2.18	942.70±451.40	12.86±2.10
	SCD	34	26.33	16	18	8.75±1.94	848.98±301.61	13.46±1.17
	Healthy controls	44	25.42	20	24	14.2±0.97	28.28±4.15	13.2±2.02
Datta et al	Thalassemia	99	23.6±10.65	30	69	6.9	2438	N/A
	IDA	33	23.6±10.65	12	21	8.2	16.4	N/A
	Chronic anaemia	18	23.6±10.65	12	6	7.07	67	N/A
Basiony et al	TDT	15	11.80±3.17	6	9	6.79±0.69	4280±1250.83	13.2 ±0.37
	Controls	15	10.20±2.96	9	6	13.67±0.57	60.70±92.46	11.93±0.42
Haghpanah et al	TDT	39	28.6 ± 6.2	12	27	9.8 ± 0.68	2694 ± 1874	15.51 ± 3.25
	Controls	27	27.1 ± 6.0,	13	14	N/A	N/A	15.33 ± 2.60
Bayramoglu et al	TDT	44	15.18±6.24	21	23	8.4±1.0	1805±15	N/A
	Controls	44	14.23±4.88	21	23	N/A	N/A	N/A

Table 36- Various Ocular and Systemic Parameters in Different Cohorts across Multiple Studies

Study	Clinical profile	Average RNFL Thickness(µm)	RNFL(S) Thickness(µm)	RNFL (I) Thickness(µm)	RNFL(N) Thickness(µm)	RNFL(T) Thickness(µm)	CMT (µm)	GLT (µm)
Aksoy et al	TDT	119.38±35.49	142.27±31.93	132.64±38.52	99.47±46.18	103.13±45.52	N/A	N/A
	IDA	184.00±31.14	174.13±49.96	171.77±58.84	200.73±60.99	189.36±36.95	N/A	N/A
	Healthy controls	187.73±27.36	181.77±21.91	198.74±28.44	186.68±39.46	184.74±37.73	N/A	N/A
Uzun et al	TDT	94 (10) *	120 (16) *	119 (26) *	66 (15) *	73 (9) *	N/A	N/A
	Controls	100 (17) *	124 (26) *	129 (25) *	79 (24) *	79 (13) *	N/A	N/A
Ulusoy et al	TDT	116.4±14.36	150.32±15.53	146.68±22.09	87.73±21.86	75.82±17.86	274.68±29.96	104.88±8.90
	SCD	108.13±10.80	134.25±17.19	137.71±17.07	85.38±18.52	72.17±13.00	265.79±184.87	98.62±8.46
	Healthy controls	123.88±9.77	162.63±21.52	153.08±8.29	99.58±26.89	76.50±19.71	275.00±23.75	105.33±7.19
Datta et al	TDT	102.17	122.37	123.85	87.68	74.78	N/A	N/A
	IDA	107.68	120.87	123	100.06	86.80	N/A	N/A
	Anaemia of chronic disorder	107.37	118.57	124	100.10	86.80	N/A	N/A
Basiony et al	TDT	100.26±1.05	125.63±14.85	122.46±15	74.67±17.6	78.3±12.94	N/A	N/A
	Controls	113.31±24.24	141.39±32.85	140.71±36.82	84.66±8.83	86.50±18.47	N/A	N/A
Haghpanah et al	Thalassemia	101.87 ±11.02	122.38 ± 24.01	137.84 ± 20.94	74.94 ± 15.55	72.35 ± 12.64	248.59 ±22.80	N/A
	Controls	99.22 ±9.95	120.51±14.56	131.29 ± 18.56	74.11 ± 12.59	70.88 ± 9.20	260 ± 21.48	N/A
Bayramoglu et al	TDT	96.43±11.01	N/A	N/A	N/A	N/A	235.79±19.22	83.23±6.35
	Controls	97.88±7.12	N/A	N/A	N/A	N/A	237.84±22.86	84.68±5.30

Median (IQR)*

Table 37- Various OCT parameters in various cohorts among various studies.

SUMMARY AND CONCLUSION

SUMMARY

A prospective cross-sectional study was conducted at a tertiary care centre over two years to compare RNFL thickness in TDT patients and normal healthy controls using SD-OCT and correlating the findings with systemic parameters like serum Hb, serum ferritin, duration of chelation, mean transfusion requirement, LIC and MIC. All patients underwent detailed history taking, their systemic parameters were recorded and a comprehensive ophthalmic examination was done to rule out the exclusion criteria. All participants were subjected to imaging using CIRRUS HDOCT 6.5 (Carl Zeiss) following pupillary dilatation. The results can be summarised as:

1. There were 85 cases (170 eyes) and 85 controls (170 eyes). The case group included 61.2% males and 38.8% females while the control group comprised of 42.4% males and 57.6% females. The mean age of the case and control group was 18.29± 6.86 and 20.87±3.24 years.
2. In the case group 95.2% of the participants had BCVA of 6/6 while in control group all 100% had BCVA of 6/6. Poor visual acuity in case group was attributed to the cortical cataracts in the case group.
3. The mean ± SD IOP in the case and control group was 14.03±2.3 mm of Hg and 14.59±2.81 mm of Hg and no statistically significant difference was noted between two groups (p=0.097).
4. The mean ± SD TBUT and Schirmer test values in the case group were 6.42±4.40 seconds and 10.91 ± 8.44 mm respectively. The mean ± SD TBUT and Schirmer test values in the control group were 8.41 ± 2.14 seconds and 12.74± 4.49 mm. There was a statistically significant difference in terms of mean TBUT and Schirmer values in the study group and controls ($p < 0.001$). The dry eye in the study group can be attributed to the squamous metaplasia of the conjunctival epithelium (goblet cell loss).

5. The mean± SD of CMT in the case and control group was 237.11± 23.94 and 236.81±21.35 µm respectively and no statically significant difference was noted between the two groups.
6. The mean ± SD of GLT in the case and control group was 84.36±5.71 µm and 82.28±7.09µm respectively. A statistically significant difference was noted between the two group with mean GLT more in the case group. Variation in findings associated with GLT needs to be further evaluated.
7. The mean ± SD of average RNFL thickness in the case and control group was 96.23 ± 9.32 and 93. 47 ± 9.68 µm and no statistically significant difference was noted between two groups.
8. The mean ± SD of the RNFL superior quadrant in cases and controls was 121.32±17.70 and 119.45± 15.67µm respectively and no significant difference was noted between the two groups.
9. The mean ± SD of the RNFL inferior quadrant in cases and control groups was 127.24 ± 15.84 µm and 122.84 ± 17.82 µm respectively and no significant difference was seen between the two groups.
10. The mean ± SD of RNFL in the temporal quadrant in cases and controls was 63.89 ± 10.15µm and 61.86± 9.69 µm respectively and no significant difference was noted between the two groups.
11. The mean ± SD of RNFL in the nasal quadrant in cases and controls was 72.31 ± 11.97µm and 69.72± 10.73µm respectively and no significant difference was noted between the same.
12. We found no correlation between any OCT parameters and systemic parameters like serum Hb, serum ferritin, average transfusion requirement, duration of chelation, LIC, and MIC.

CONCLUSION

This study compared the RNFL thickness in patients with TDT and healthy controls. Our findings highlight no significant differences in RNFL thickness in TDT patients as previously reported by other studies. We found no correlation of RNFL thickness and systemic parameters like serum ferritin, serum Hb levels, average transfusion requirement, LIC and MIC. In our study, TDT patients had low tear film parameters like TBUT and Schirmer test values confirming the presence of ocular surface disease in these patients. Thus, these patients require regular ophthalmic examinations to prevent any long term sequalae.

STRENGTHS OF OUR STUDY

1. Large sample size of our study as compared to previous studies.
2. All measurements were performed by a single, trained observer reducing inter-observer variability.
3. Comprehensive ocular examination including parameters like TBUT and Schirmer test was additionally performed and analyzed.
4. Correlation of systemic parameters and ocular parameters.

LIMITATIONS

1. Systemic parameters such as serum ferritin, liver iron concentration, and cardiac MRI were not assessed in the control group.
2. A cross-sectional study design is another limitation of this study as longitudinal follow-up study would provide more comprehensive insights into the progression of retinal changes.
3. The study did not include measurements of axial length, which can influence the accuracy of retinal nerve fibre thickness measurements, potentially affecting the results.

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KEY TO MASTER CHART

Gender

1- Male
2- Female

Education

0- Nil
1- Preschool
2- Primary school
3- Lower secondary
4- Upper secondary
5- Higher education

History of consanguinity

0- No
1- Yes

Co-existent endocrinal disorder

0- No
1- Yes

Transfusion transmitted infection

0- No
1- Hepatitis-B

2- Hepatitis-C
3- HIV

Type of chelation

0- Desferoxamine
1- Deferiperone
2- Deferasirox
3- Desferoxamine+deferiprone
4- Deferiprone+deferasirox
5- Desferoxamine+deferasirox

Severity of LIC

0- Normal
1- Mild
2- Moderate
3- Severe

Severity of MIC

0- Normal
1- Mild
2- Moderate
3- Severe

S. No.	NAME	AGE (YEARS)	GENDER	EDUCATION	GPE					Clinical Profile					
					SYSTOLIC BP (MMHG)	DIASTOLIC BP (MMHG)	RR/MIN	SPO2	HR/MIN	AGE AT DIAGNOSIS (MONTHS)	H/O CONSANGUINITY	COMMENT ON CSG	CO-EXIST ENDOCRINAL DS	COMMENT ON ENDO DISEASE	CO-EXISTENT INFECTION
1	DV	17	1	4	110	70	24	97	84	12	0		0		0
2	PS	18	1	5	120	60	24	98	110	4	0		0		0
3	V	10	1	2	110	70	25	98	98	14	0		0		0
4	VG	13	2	3	110	80	24	99	84	3	0		1	HYPOTHYROIDISM	0
5	U	24	1	5	120	80	23	98	92	4	0		1	HYPOTHYROIDISM,DIABETES MELLITUS	0
6	SS	19	1	5	120	80	26	99	85	7	0		0		0
7	S	11	1	3	120	90	24	98	89	1	0		0		0
8	SS	26	1	5	110	90	25	99	87	36	0		0		0
9	S	17	2	4	120	90	25	98	84	36	0		1	HYPOTHYROIDISM	0
10	S	30	1	5	110	90	27	97	82	5	0		1	HYPOTHYROIDISM	2
11	S	20	2	5	120	90	25	97	84	12	0		1	HYPOTHYROISM, DELAYED PUBERTY	0
12	S	11	1	3	110	90	24	99	87	17	0		0		0
13	S	15	1	4	110	90	23	98	85	8	0		0		0
14	R	14	2	3	120	80	24	98	83	22	0		0		0
15	R	20	1	5	120	80	26	97	84	18	0		0		0
16	R	12	2	3	120	90	24	99	88	7	0		0		0
17	PK	21	2	5	110	90	27	98	84	24	0		1	HYPOTHYROIDISM	0
18	R	9	2	2	100	70	25	99	87	96	1		1	HYPOTHYROIDISM	0
19	R	18	1	5	110	90	24	98	82	24	0		0		0
20	RM	23	2	5	110	80	23	99	84	12	0		1	HYPOTHYROIDISM	0
21	R	14	2	3	110	80	24	97	82	30	1		0		0
22	VS	13	1	**3**	100	80	27	99	73	3	0		0		0
23	GG	23	1	5	100	70	24	98	84	8	0		0		0
24	GS	21	1	5	110	80	24	99	84	7	0		1	HYPOTHYROIDISM	0
25	G	7	2	2	120	70	25	98	86	10	0		0		0
26	H	18	1	5	110	80	26	97	87	10	0		1	HYPOTHYROIDISM	0
27	H	17	1	4	100	80	24	98	86	1	0		0		0
28	H	15	1	3	110	70	25	98	87	7	0		0		0
29	IH	23	2	5	120	80	25	98	93	132	0		0		0
30	IS	12	1	3	100	80	25	98	86	8	0		1	HYPOTHYROIDISM	0
31	J	18	1	5	100	90	24	99	87	8	0		0		0
32	JK	19	2	5	120	90	25	98	92	3	0		0		0
33	JS	7	1	2	110	70	26	97	87	30	0		0		0
34	JK	27	2	5	120	70	24	98	84	36	0		0		0
35	J	6	2	2	110	80	23	97	86	8	0		0		0
36	J	16	2	4	110	70	25	98	87	36	0		1	HYPOTHYROIDISM	0
37	JK	21	2	5	120	90	24	99	82	4	0		0		0
38	J	19	1	5	110	80	24	98	85	30	0		1	HYPOTHYROIDISM	0
39	J	16	1	4	120	90	23	99	84	4	0		1	HYPOTHYROIDISM	0
40	A	14	1	3	120	90	24	99	84	28	0		1	HYPOTHYROIDISM	0
41	GS	20	1	5	120	80	23	97	87	7	0		1	HYPOTHYROIDISM	0
42	K	16	1	4	100	70	27	98	85	4	0		0		0
43	EK	24	2	5	120	70	24	97	84	6	0		0		2
44	D	11	1	3	110	70	25	98	97	9	0		0		0
45	AN	9	1	2	110	80	25	99	86	8	0		0		0
46	B	26	2	5	100	70	24	98	87	11	0		1	DELAYED PUBERTY	0

S. No.	Transfusion Profile					Investigations					Ocu				
	AGE OF INITIATING TRANSFUSION (IN MONTHS)	TYPE OF CHELATION	DURATION OF CHELATION (IN YEARS)	AVG HG OVER 5 YEARS	AVG TRANSFUSION REQ. OVER 5 YRS-ML	SERUM FERRITIN LEVELS	LIC	SEVERITY OF LIC	CARDIAC MRI	SEVERITY OF MIC	BCVA(R/E)	BCVA(L/E)	CV(R/E)	CV(L/E)	IOP(R/E)
1	3	2	14	9.5	200	2718	1.64	0	0.74	0	6/6	6/6	N	N	10
2	3	4	16	8.4	212	4730	22.4	3	0.51	0	6/6	6/6	N	N	15
3	2	4	6	9.6	268	4469	N/A	N/A	N/A		6/6	6/6	N	N	10
4	3	4	6	9.2	165	3229	24.25	3	0.88	0	6/6	6/6	N	N	18
5	4	4	15	9.2	268	3554	9.14	2	0.56	0	6/6	6/6	N	N	17
6	7	4	14	8.7	250	1606	16.14	3	0.72	0	6/6	6/6	N	N	14
7	1	4	10	9.6	133	911	N/A	N/A	N/A		6/6	6/6	N	N	16
8	36	4	15	9.2	288	3801	33.23	3	1.72	2	6/6	6/6	N	N	17
9	36	3	15	9.2	298	1054	9.07	2	9.2	3	6/6	6/6	N	N	16
10	5	5	22	9.4	268	4222	9.66	2	0.47	0	6/6	6/6	RED-GREEN DEFECT	RED GREEN DEFECT	15
11	12	4	15	9.4	223	2586	11.8	2	0.48	0	6/6	6/6	N	N	16
12	12	2	6	9.4	255	1487	N/A	N/A	N/A		6/6	6/6	N	N	14
13	8	2	12	9.2	143	914	7.25	2	0.48	0	6/6	6/6	RED GREEN DEFECT	RED GREEN DEFECT	17
14	22	4	5	9.3	154	687	3.16	1	0.35	0	6/6	6/6	N	N	14
15	18	5	18	8.9	268	2119	16.27	3	0.51	0	6/6p	6/6p	N	N	17
16	7	4	8	9.2	173	5674	9.59	2	0.55	0	6/6	6/6	N	N	18
17	36	4	16	9.2	233	4490	N/A	N/A	N/A		6/6	6/6	N	N	12
18	96	2	1	8.5	120	559	N/A	N/A	N/A		6/6	6/6	N	N	18
19	15	4	15	9.4	140	3593	16.16	3	1.39	1	6/6	6/6	N	N	12
20	12	2	16	9.5	213	1074	5.95	1	0.72	0	6/9	6/9	N	N	12
21	30	4	8	8.9	114	1318	N/A	N/A	N/A		6/6	6/6	N	N	20
22	3	2	4	9.5	226	3167	17.24	3	1.66	2	6/6	6/6	N	N	14
23	8	4	16	9.4	213	1932	4.93	1	0.8	0	6/6	6/6	N	N	15
24	7	4	15	8.6	224	2211	28.02	3	0.54	0	6/6	6/6	N	N	14
25	10	2	2	9.6	184	1740	N/A	N/A	N/A		6/6	6/6	N	N	12
26	10	2	15	9	214	886	6.56	1	0.4	0	6/6	6/6	N	N	17
27	1	2	14	9.6	130	2010	N/A	N/A	N/A		6/6	6/6	N	N	12
28	7	2	13	9.5	237	920	3.21	1	0.58	0	6/6	6/6	N	N	13
29	120	2	3	8.4	130	704	N/A	N/A	N/A		6/6	6/6	N	N	14
30	8	4	14	8.3	160	1154	2.8	1	22	3	6/6	6/6	N	N	12
31	8	2	15	9.2	134	857	5.33	1	0.53	0	6/6	6/6	N	N	17
32	3	4	10	9	211	3032	N/A	N/A	N/A		6/6	6/6	N	N	17
33	30	2	5	9.1	130	1096	N/A	N/A	N/A		6/6	6/6	N	N	12
34	36	4	15	9.12	211	2462	18.17	3	0.37	0	6/6	6/6	N	N	18
35	8	2	2	8.6	131	3999	N/A	N/A	N/A		6/6	6/6	N	N	13
36	36	5	9	7.9	273	3710	N/A	N/A	N/A		6/6	6/6	N	N	15
37	4	4	15	9.5	273	2016	8.4	2	0.94	0	6/6	6/6	N	N	18
38	30	4	15	8.8	284	5120		N/A	0.29	0	6/6	6/6	N	N	14
39	2	2	8	9.2	258	1316	2.67	1	0.49	0	6/6	6/6	N	N	13
40	24	4	10	8.9	268	2146	N/A	N/A	N/A		6/6	6/6	N	N	13
41	7	4	15	8.6	242	3945	28.02	3	0.54	0	6/6	6/6	N	N	12
42	4	2	13	9	142	1786	N/A	N/A	N/A		6/6	6/6	N	N	12
43	6	2	21	8.7	225	4298	7.08	2	0.68	0	6/6	6/6	N	N	13
44	9	2	9	9.5	213	1540	1.94	0	0.47	0	6/6	6/6	N	N	12
45	8	4	8	8.9	225	4529	N/A	N/A	N/A		6/6	6/6	N	N	13
46	11	4	15	9.8	213	3665	36.29	3	1.14	0	6/6	6/6	N	N	11

S. No.	ar Examination					OCT Features											
	IOP(L/E)	TBUT(R/E)TBUT(L/E)		SCHIRMER(R/E)	SCHIRMER(L/E)	CMT(R/E)	CMT(L/E)	GLT(R/E)	GLT(L/E)	RNFL(S)(R/E)	RNFL(S)(L/E)	RNFL(I)(R/E)	RNFL(I)(L/E)	RNFL(T)(R/E)	RNFL(T)(L/E)	RNFL(N)(R/E)	RNFL(N)(L/E)
1	10	7	5	3	4	302	297	84	84	131	124	123	121	57	51	57	61
2	13	16	18	16	17	248	242	86	84	126	119	135	129	71	56	82	82
3	12	16	17	22	28	232	236	82	80	106	120	125	106	56	65	64	56
4	12	10	12	7	8	230	226	85	85	88	97	106	112	79	70	66	62
5	14	4	4	2	5	237	241	79	82	141	123	132	133	69	64	58	56
6	13	5	6	10	15	260	251	94	93	146	145	147	135	77	72	90	91
7	18	4	6	12	14	251	250	80	80	130	123	122	121	57	64	66	53
8	18	4	5	20	18	298	296	75	66	108	107	143	143	58	59	83	84
9	15	6	5	11	8	218	214	88	89	125	136	106	106	76	63	66	78
10	16	7	7	16	17	283	279	89	89	121	124	136	139	65	60	91	91
11	17	8	9	14	16	232	237	93	95	130	126	149	153	63	66	84	85
12	13	5	6	10	7	244	243	81	83	135	133	135	135	66	68	67	70
13	13	3	4	5	3	244	243	81	83	135	133	135	135	66	68	67	70
14	16	4	6	12	15	232	231	87	87	163	168	196	159	112	90	59	61
15	19	4	6	3	4	224	227	72	91	134	134	105	135	66	75	92	83
16	19	5	3	35	35	228	218	86	86	117	125	143	136	84	69	52	57
17	14	6	7	10	13	267	261	81	80	112	119	112	104	49	50	68	75
18	19	4	5	16	17	247	248	84	85	123	122	112	128	73	66	68	68
19	10	3	4	5	2	259	267	92	93	129	134	137	133	72	73	68	76
20	12	5	6	3	4	238	239	86	87	113	117	122	128	63	66	69	72
21	17	5	7	1	6	261	264	93	93	157	133	131	126	64	59	87	75
22	13	10	10	25	25	227	226	91	91	149	156	139	134	62	63	80	78
23	16	2	3	7	8	222	225	85	84	117	112	121	123	62	52	68	81
24	14	3	4	5	4	246	252	89	89	119	124	128	126	65	72	80	62
25	13	5	6	7	9	212	221	88	88	82	155	142	157	89	70	76	83
26	18	5	3	7	8	263	243	81	82	129	119	131	111	55	58	69	76
27	14	14	16	20	20	206	232	71	72	105	115	132	130	45	36	66	65
28	14	9	9	10	10	234	238	82	81	140	152	151	164	51	45	80	81
29	13	30	30	25	35	262	262	77	75	101	98	119	112	63	65	52	48
30	13	14	5	12	11	237	237	89	90	118	111	132	129	65	60	86	91
31	15	4	3	9	7	236	236	84	85	116	126	128	128	54	53	69	80
32	15	4	3	9	7	246	254	86	87	128	136	128	130	58	53	82	76
33	16	3	5	6	9	243	249	93	92	146	120	112	120	60	63	103	84
34	14	4	7	14	8	244	246	82	83	125	116	116	108	61	71	76	55
35	15	4	6	12	13	201	201	84	85	96	126	130	142	59	54	88	81
36	16	20	5	15	14	208	207	84	80	110	97	137	127	60	64	75	71
37	18	6	13	10	5	239	232	86	84	106	116	117	122	77	71	64	69
38	15	8	9	10	15	271	266	87	90	129	136	159	140	55	62	91	95
39	13	12	13	25	25	248	233	76	82	117	143	117	130	52	53	89	90
40	14	2	4	3	6	236	242	91	89	138	145	135	144	58	60	84	86
41	14	3	6	5	6	249	249	80	90	124	126	132	132	66	70	83	69
42	13	6	8	10	10	218	222	85	88	144	127	138	141	81	73	76	56
43	15	6	8	12	14	240	244	84	86	120	145	140	148	69	66	94	102
44	13	14	15	10	9	245	256	92	91	165	148	140	138	67	68	66	68
45	14	3	4	9	7	225	214	81	79	157	125	148	118	66	54	57	73
46	10	13	3	3	3	202	201	79	80	135	121	142	137	60	66	83	84

S. No.	NAME	AGE (YEARS)	GENDER	EDUCATION	GPE					Clinical Profile					
					SYSTOLIC BP (MMHG)	DIASTOLIC BP (MMHG)	RR/MIN	SPO2	HR/MIN	AGE AT DIAGNOSIS (MONTHS)	H/O CONSANGUINITY	COMMENT ON CSG	CO-EXIST ENDOCRINAL DS	COMMENT ON ENDO DISEASE	CO-EXISTENT INFECTION
47	AK	30	1	5	110	80	25	99	86	324	0		1	HYPOTHYROIDISM,HYPOPARATHYROIDISM	0
48	A	6	1	2	110	90	24	98	86	48	0		0		0
49	AS	26	1	5	120	90	25	97	86	4	0		1	HYPOTHYROIDISM	0
50	A	30	1	5	120	90	24	99	85	36	0		1	HYPOTHYROIDISM,DIABETES MELLITUS,DELAYED PUBERTY	0
51	AS	28	1	5	120	70	25	98	84	60	0		1	DIABETES MELLITUS	0
52	A	13	1	3	110	70	24	98	85	9	0		0		0
53	A	11	2	3	120	70	27	99	92	12	0		0		0
54	BK	16	2	4	110	70	24	97	84	5	1	MARRIED TO MATERNAL AUNT'S SIBLING	0		0
55	A	13	2	3	110	90	24	98	92	9	0		0		0
56	AK	12	2	3	120	90	27	98	84	48	0		0		0
57	AS	11	1	3	110	70	24	98	84	13	0		0		0
58	G	9	1	2	100	70	25	97	82	6	0		0		0
59	K	7	1	2	120	70	24	98	85	6	0		0		0
60	K	18	2	4	110	70	25	97	84	8	0		0		0
61	K	21	2	5	100	70	30	98	100	7	0		1	HYPOTHYROIDISM,DELAYED PUBERTY	0
62	A	28	1	5	110	70	26	98	84	10	0		1	HYPOTHYROIDISM,DELAYED PUBERTY	2
63	K	19	1	4	110	70	31	99	84	7	0		0		0
64	G	10	2	2	100	70	24	98	80	120	0		0		0
65	K	25	1	5	120	70	24	97	84	10	0		0		0
66	MM	16	1	4	100	70	24	98	84	3	0		0		0
67	M	28	2	5	110	70	26	98	100	5	0		1	HYPOTHYROIDISM	0
68	GS	27	1	5	100	80	24	97	85	5	0		1	HYPOTHYROIDISM	0
69	M	29	1	5	120	70	25	98	87	12	0		1	HYPOTHYROIDISM	0
70	MK	9	2	2	110	70	24	97	98	48	0		0		0
71	MD	30	1	5	110	70	24	98	100	96	0		0		0
72	N	21	1	5	100	70	24	98	85	8	0		0		0
73	AS	18	1	4	110	80	24	99	84	12	0		0		0
74	NS	14	1	3	120	70	25	97	85	5	0		0		0
75	P	21	2	5	120	70	26	98	84	8	0		0		0
76	P	13	2	3	110	70	24	97	25	17	0		1	HYPOTHYROIDISM	2
77	P	28	1	5	100	70	25	98	85	8	0		1	HYPOTHYROIDISM	0
78	AS	15	1	4	100	70	25	97	86	7	0		1	HYPOTHYROIDISM	0
79	SK	30	2	5	110	70	24	97	85	42	0		0		2
80	RK	30	1	5	120	70	24	98	84	24	0		0		2
81	R	30	1	5	120	70	25	97	95	24	0		1	HYPTHYROIDISM,DELAYED PUBERTY	0
82	R	25	1	5	110	70	24	97	84	18	0		0		0
83	AS	24	2	5	120	80	26	99	87	84	0		1	HYPOTHYROIDISM	0
84	RV	13	2	3	110	70	25	99	84	11	1		0		0
85	V	21	2	5	100	70	24	99	85	15	0		1	HYPOTHYROIDISM,TYPE2 DIABETES	0

S. No.	Transfusion Profile					Investigations					Ocu				
	AGE OF INITIATING TRANSFUSION (IN MONTHS)	TYPE OF CHELATION	DURATION OF CHELATION (IN YEARS)	AVG HG OVER 5 YEARS	AVG TRANSFUSION REQ. OVER 5 YRS-ML	SERUM FERRITIN LEVELS	LIC	SEVERITY OF LIC	CARDIAC MRI	SEVERITY OF MIC	BCVA(R/E)	BCVA(L/E)	CV(R/E)	CV(L/E)	IOP(R/E)
47	27	4	4	9.3	242	1768	31	3	7.85	3	6/6	6/6	N	N	11
48	36	4	1	9.4	231	3711	N/A	N/A	N/A		6/6	6/6	N	N	11
49	4	5	15	9	243	3397	25.84	3	1.46	1	6/6	6/6	N	N	11
50	36	4	22	8.4	165	3649	N/A	N/A	N/A		6/6	6/6	N	N	14
51	60	4	7	8.9	134	415	5.71	1	5.78	3	6/6	6/6	N	N	12
52	9	4	11	9.5	166	2154	N/A	N/A	N/A		6/6	6/6	N	N	12
53	8	2	2	9.5	431	2000	N/A	N/A	N/A		6/6	6/6	N	N	14
54	5	2	14	9	234	1035	1.34	0	0.51	0	6/6	6/6	N	N	12
55	9	2	10	9.3	123	898	N/A	N/A	N/A		6/6	6/6	N	N	20
56	48	2	3	9.2	227	2147	N/A	N/A	N/A		6/6	6/6	N	N	12
57	36	2	9	9	134	1391	0.96	0	0.5	0	6/6	6/6	N	N	12
58	6	4	6	9.3	236	4915	N/A	N/A	N/A		6/6	6/6	N	N	12
59	6	2	4	9.2	92	2919	N/A	N/A	N/A		6/6	6/6	N	N	12
60	8	2	15	9.5	227	1676	3.58	1	0.56	0	6/6	6/6	N	N	15
61	14	5	15	9.3	230	6072	12.2	2	0.95	0	6/6	6/6	N	N	14
62	10	4	16	9.6	289	1884	11.32	2	1.07	0	6/6	6/6	N	N	12
63	7	4	14	8.7	143	1039	18.35	3	1.65	1	6/6	6/6	N	N	10
64	120	2	0	9.2	133	207	3.1	1	0.9	0	6/6	6/6	N	N	13
65	10	2	15	9.3	213	912	8.24	2	0.63	0	6/6	6/6	N	N	12
66	4	2	14	8.9	243	963	1.8	0	0.58	0	6/6	6/6	N	N	12
67	5	4	22	10	268	2488	4.7	1	5.64	2	6/9	6/9	N	N	10
68	5	4	22	8.7	256	5769	49.5	3	1.13	0	6/6	6/6	N	N	21
69	12	4	22	9.2	187	2735	4.51	1	0.54	0	6/6	6/6	N	N	10
70	48	2	3	9.2	266	1066	N/A	N/A	N/A		6/6	6/6	N	N	12
71	96	4	19	9.4	234	1516	0.72	0	1.1	0	6/6	6/6	N	N	13
72	8	4	19	8.4	214	3879	1.05	0	1.2	0	6/6	6/6	N	N	13
73	12	4	10	8.5	231	1468	15.45	3	0.55	0	6/6	6/6	N	N	17
74	4	4	9	8.5	170	2733	4.74	1	0.54	0	6/6	6/6	N	N	15
75	8	2	15	9	189	1288	3.3	1	5.5	3	6/6	6/6	N	N	17
76	17	4	10	9.1	236	6907	N/A	N/A	N/A		6/6	6/6	N	N	10
77	8	2	15	8.5	133	1819	N/A	N/A	N/A		6/6	6/6	N	N	13
78	7	4	11	9.2	278	3025	20.8	3	0.7	0	6/6p	6/6p	N	N	12
79	42	4	15	9.7	267	3350	9.79	2	0.78	0	6/6	6/6	N	N	12
80	24	4	17	9.3	234	2242	5.38	1	3.3	3	6/6	6/6	N	N	14
81	24	4	15	9.5	214	1305	1.45	0	0.63	0	6/6	6/6	N	N	15
82	30	4	19	8.6	234	1232	17.41	3	0.4	0	6/6	6/6	N	N	16
83	84	5	14	9.3	231	3082	8.31	2	0.3	0	6/6	6/6	N	N	14
84	11	4	10	11.4	234	3349	N/A	N/A	N/A		6/6	6/6	N	N	12
85	15	4	18	8.28	278	14177	26.26	3	9.24	3	6/6	6/6	N	N	10

S. No.	ar Examination					OCT Features											
	IOP(L/E)	TBUT(R/E)TBUT(L/E)		SCHIRMER(R/E)	SCHIRMER(L/E)	CMT(R/E)	CMT(L/E)	GLT(R/E)	GLT(L/E)	RNFL(S)(R/E)	RNFL(S)(L/E)	RNFL(I)(R/E)	RNFL(I)(L/E)	RNFL(T)(R/E)	RNFL(T)(L/E)	RNFL(N)(R/E)	RNFL(N)(L/E)
47	11	2	3	1	4	218	222	93	92	124	126	153	142	80	66	62	78
48	13	5	6	6	7	232	241	94	90	162	176	154	154	80	69	73	77
49	12	3	4	10	10	243	244	74	75	117	123	114	110	47	47	64	60
50	16	6	7	13	10	264	240	81	80	128	111	130	108	72	77	80	77
51	13	10	10	35	35	232	222	82	82	124	129	132	131	53	48	59	53
52	13	5	8	17	14	296	300	82	83	77	84	120	112	49	42	71	67
53	15	5	5	15	16	233	323	90	90	101	114	146	136	81	71	87	94
54	13	10	12	35	30	223	230	83	82	119	136	115	121	77	64	57	61
55	17	2	4	3	6	224	229	83	82	117	118	109	123	45	47	87	90
56	13	6	7	3	4	231	230	82	82	122	125	136	136	81	71	68	66
57	13	3	4	7	5	206	208	78	75	106	92	89	80	57	61	58	54
58	15	4	6	3	5	242	233	97	96	132	144	109	114	81	81	61	57
59	14	4	5	12	3	256	250	93	92	124	137	142	152	74	72	92	85
60	16	3	4	5	6	212	213	86	85	132	144	172	152	88	77	68	78
61	15	3	2	1	4	217	213	88	86	153	168	129	129	73	70	78	60
62	13	4	5	12	13	250	248	87	86	99	99	111	106	54	59	72	66
63	15	7	9	14	18	218	221	85	86	150	141	135	150	63	71	65	71
64	14	3	4	5	7	192	200	82	83	137	133	135	131	71	68	70	71
65	14	3	9	4	6	201	205	84	82	95	100	109	113	79	73	60	61
66	13	4	5	6	8	235	254	91	89	132	131	152	142	67	65	67	71
67	14	4	5	12	13	217	211	81	81	129	113	104	109	78	73	52	56
68	19	10	11	35	35	242	251	80	80	87	90	97	92	55	57	67	57
69	10	9	4	3	5	236	232	82	80	117	121	124	114	71	73	62	59
70	14	3	4	5	5	214	213	87	88	114	128	124	124	61	59	79	78
71	14	4	5	5	6	261	258	87	87	125	135	128	123	70	69	76	80
72	14	1	2	3	4	212	206	86	87	119	119	117	118	62	60	76	73
73	16	3	3	4	1	193	200	72	74	127	116	105	118	60	54	82	90
74	14	3	4	5	6	235	240	88	92	113	125	126	137	81	69	77	75
75	16	2	3	4	3	249	255	74	74	109	94	123	121	70	74	42	38
76	12	9	9	15	16	246	246	83	83	122	106	98	114	51	57	69	56
77	14	10	12	35	35	207	210	74	73	101	104	110	98	66	74	58	59
78	13	4	5	4	7	262	262	80	78	131	116	112	118	68	60	61	66
79	12	3	4	5	9	219	223	88	87	118	101	147	175	58	62	85	76
80	13	7	4	3	4	209	207	83	86	138	112	119	124	66	61	76	67
81	16	8	9	19	17	252	249	89	90	136	131	139	136	70	70	80	72
82	16	3	4	5	20	293	290	86	85	118	126	156	150	59	59	85	76
83	13	7	4	7	6	220	219	80	78	108	108	123	122	54	53	75	68
84	14	5	6	4	6	212	221	88	88	82	155	142	157	89	70	76	83
85	12	3	4	6	3	193	200	72	74	136	138	139	122	52	45	79	69

S. No.	NAME	AGE (YEARS)	GENDER	EDUCATION	GPE					Ocular Examination								
					SYSTOLIC BP (MMHG)	DIASTOLIC BP (MMHG)	RR/MIN	SPO2	HR/MIN	BCVA(R/E)	BCVA(L/E)	CV(R/E)	CV(L/E)	IOP(R/E)	IOP(L/E)	TBUT(R/E)TBUT(L/E)		SCHIRMER(R/E)
1	H	21	2	5	110	70	24	99	84	6/6	6/6	N	N	17	11	10	9	18
2	K	23	2	5	120	80	21	98	83	6/6	6/6	N	N	16	17	9	8	16
3	K	21	2	5	110	70	20	99	85	6/6	6/6	N	N	12	13	8	9	15
4	K	22	2	5	90	60	23	98	84	6/6	6/6	N	N	17	16	10	8	14
5	K	23	2	5	120	70	24	97	83	6/6	6/6	N	N	12	13	9	8	10
6	MV	20	2	5	110	70	20	99	85	6/6	6/6	N	N	16	17	7	8	9
7	M	25	1	5	120	80	24	99	83	6/6	6/6	RED GREEN DEFECT	RED GREEN DEFECT	17	11	10	9	10
8	M	25	1	5	110	90	21	97	84	6/6	6/6	N	N	12	16	7	8	25
9	M	20	1	5	120	70	20	99	83	6/6	6/6	N	N	17	13	6	7	8
10	N	20	1	5	100	80	21	98	85	6/6	6/6	N	N	16	17	10	9	6
11	N	20	2	5	120	80	20	97	84	6/6	6/6	N	N	17	16	8	9	10
12	N	19	1	5	110	70	22	98	85	6/6	6/6	N	N	13	11	6	7	12
13	P	17	2	4	110	90	24	99	83	6/6	6/6	N	N	12	16	10	9	14
14	PS	20	1	5	120	70	20	97	84	6/6	6/6	N	N	17	17	9	8	18
15	P	23	1	5	100	80	24	98	84	6/6	6/6	N	N	13	16	8	9	19
16	P	21	2	5	90	60	24	99	85	6/6	6/6	N	N	11	12	7	8	20
17	P	21	2	5	120	80	21	98	83	6/6	6/6	N	N	17	16	5	6	23
18	R	7	1	2	110	70	23	97	84	6/6	6/6	N	N	10	17	6	7	8
19	RC	21	1	5	120	80	20	99	85	6/6	6/6	N	N	9	16	12	10	9
20	R	23	1	5	120	70	24	98	83	6/6	6/6	N	N	17	13	15	10	10
21	R	22	1	5	100	70	21	97	84	6/6	6/6	N	N	11	17	10	9	14
22	R	20	2	5	100	80	22	99	85	6/6	6/6	N	N	17	11	17	10	16
23	R	19	2	5	120	80	24	97	85	6/6	6/6	N	N	17	13	9	8	18
24	RK	21	2	5	110	70	20	98	83	6/6	6/6	N	N	11	16	10	9	19
25	R	21	2	5	120	70	24	99	84	6/6	6/6	N	N	13	17	8	7	20
26	S	21	2	5	90	60	21	97	85	6/6	6/6	N	N	17	12	7	8	21
27	S	20	2	5	120	80	20	98	83	6/6	6/6	N	N	11	16	6	8	25
28	S	18	1	4	110	70	22	97	84	6/6	6/6	N	N	12	10	12	10	24
29	SS	20	1	5	110	70	21	99	85	6/6	6/6	N	N	16	17	16	10	21
30	S	18	2	4	110	90	24	99	84	6/6	6/6	N	N	17	13	10	9	15
31	S	24	1	5	100	80	20	98	85	6/6	6/6	N	N	12	11	6	7	16
32	S	10	1	2	120	80	21	99	83	6/6	6/6	N	N	10	21	5	8	18
33	S	20	2	5	110	70	24	98	84	6/6	6/6	N	N	13	16	3	4	19
34	S	21	2	5	110	90	20	99	85	6/6	6/6	N	N	16	17	6	8	20
35	S	22	2	5	120	70	21	97	83	6/6	6/6	N	N	17	11	15	10	12
36	SK	21	2	5	110	70	24	98	84	6/6	6/6	N	N	10	16	10	9	16
37	SK	23	2	5	120	80	20	99	85	6/6	6/6	N	N	11	21	7	8	14
38	SS	27	1	5	110	90	21	97	83	6/6	6/6	N	N	12	16	8	9	12
39	V	19	2	5	120	70	22	98	84	6/6	6/6	N	N	17	13	10	9	16
40	RS	24	1	5	120	80	24	99	85	6/6	6/6	N	N	11	17	6	7	18
41	GS	21	1	5	110	70	20	98	83	6/6	6/6	N	N	10	16	12	10	12
42	DD	25	1	5	100	80	21	99	85	6/6	6/6	N	N	17	12	7	8	10
43	B	22	2	5	90	60	22	98	84	6/6	6/6	N	N	16	11	8	9	12
44	B	22	1	5	100	80	23	99	84	6/6	6/6	N	N	13	17	10	9	15

S. No.		OCT Features											
	SCHIRMER(L/E)	CMT(R/E)	CMT(L/E)	GLT(R/E)	GLT(L/E)	RNFL(S)(R/E)	RNFL(S)(L/E)	RNFL(I)(R/E)	RNFL(I)(L/E)	RNFL(T)(R/E)	RNFL(T)(L/E)	RNFL(N)(R/E)	RNFL(N)(L/E)
1	17	222	234	76	80	141	118	134	130	66	59	54	55
2	15	215	223	83	85	125	121	135	130	58	58	63	64
3	14	213	216	79	77	114	113	117	110	55	53	59	63
4	12	193	191	73	74	117	117	113	114	50	42	73	67
5	9	215	214	83	84	115	119	116	118	78	78	87	80
6	10	220	222	83	84	123	136	129	142	63	51	59	69
7	12	270	271	82	82	104	111	106	102	58	57	76	66
8	24	299	299	83	73	98	101	129	119	83	74	77	72
9	6	263	260	78	40	107	120	121	119	60	55	90	94
10	8	251	246	82	82	120	135	124	138	68	61	71	68
11	12	236	245	84	85	132	121	140	128	74	57	75	91
12	10	253	248	83	83	111	128	113	122	61	62	65	62
13	15	252	242	80	81	98	90	113	126	52	57	62	62
14	18	224	227	84	84	110	105	115	132	55	48	50	55
15	20	241	263	88	84	136	144	143	130	60	55	87	86
16	24	227	226	84	82	127	129	118	127	60	48	69	59
17	21	247	258	73	59	95	112	102	94	53	53	71	63
18	9	247	235	83	84	114	127	115	116	53	54	64	61
19	10	251	252	94	94	153	165	156	143	60	61	76	79
20	12	234	225	80	82	108	131	119	132	52	53	64	70
21	16	241	248	84	85	122	118	140	133	56	61	68	63
22	17	188	190	74	76	85	94	91	94	44	46	59	51
23	19	198	187	86	85	139	127	129	141	77	66	70	78
24	18	258	259	82	82	112	124	102	110	84	67	51	53
25	19	216	230	84	83	129	141	123	117	67	63	66	61
26	20	219	217	84	87	126	126	130	131	65	53	70	87
27	24	224	246	72	68	64	64	58	53	54	45	72	57
28	20	260	259	85	85	108	108	121	121	60	51	70	67
29	19	243	242	86	88	123	134	132	123	59	59	75	70
30	14	208	208	84	84	127	123	130	135	66	60	69	69
31	14	241	248	97	96	116	117	149	147	89	93	74	63
32	16	231	241	81	82	119	125	140	136	63	55	82	90
33	17	214	215	77	76	118	107	135	111	57	48	67	74
34	18	260	246	87	88	118	128	146	116	73	77	75	65
35	10	209	212	82	82	125	129	122	124	68	68	78	85
36	14	212	209	93	79	127	131	142	125	61	63	70	63
37	12	206	232	58	82	115	115	120	124	64	65	62	67
38	10	248	242	86	85	108	114	107	101	67	67	61	64
39	18	252	254	97	96	112	129	186	193	101	86	73	82
40	16	250	254	76	81	108	111	100	102	55	54	74	74
41	10	251	250	79	78	117	126	121	132	68	64	68	65
42	12	226	204	79	63	100	81	100	114	63	53	55	58
43	10	274	272	87	86	112	105	114	107	47	55	69	68
44	16	230	230	75	75	135	129	117	119	74	61	58	67

S. No.	NAME	AGE (YEARS)	GENDER	EDUCATION	GPE					Ocular Examination								
					SYSTOLIC BP (MMHG)	DIASTOLIC BP (MMHG)	RR/MIN	SPO2	HR/MIN	BCVA(R/E)	BCVA(L/E)	CV(R/E)	CV(L/E)	IOP(R/E)	IOP(L/E)	TBUT(R/E)TBUT(L/E)		SCHIRMER(R/E)
45	A	23	2	5	120	80	24	99	85	6/6	6/6	N	N	10	17	4	3	10
46	HD	23	1	5	100	80	20	98	84	6/6	6/6	N	N	11	16	5	6	14
47	G	26	1	5	120	70	21	97	84	6/6	6/6	N	N	17	13	8	9	17
48	Y	26	2	5	110	90	24	98	85	6/6	6/6	N	N	16	12	10	7	18
49	DD	19	2	5	100	80	21	99	85	6/6	6/6	N	N	13	11	9	10	10
50	C	22	2	5	120	80	20	97	84	6/6	6/6	N	N	12	16	12	10	9
51	B	24	2	5	110	70	21	98	85	6/6	6/6	N	N	11	13	6	8	7
52	AS	18	1	4	120	70	24	99	83	6/6	6/6	N	N	17	12	8	9	8
53	AS	20	1	5	100	80	20	97	84	6/6	6/6	N	N	21	17	10	11	9
54	AS	24	1	5	90	60	22	98	85	6/6	6/6	N	N	11	12	8	9	10
55	A	22	2	5	120	80	21	97	85	6/6	6/6	N	N	17	12	9	10	9
56	A	23	1	5	110	90	24	99	84	6/6	6/6	N	N	13	11	6	7	8
57	A	20	1	5	100	80	20	99	85	6/6	6/6	N	N	12	17	10	9	10
58	A	23	1	5	120	70	21	97	85	6/6	6/6	N	N	11	16	8	5	9
59	GK	20	2	5	120	80	22	98	84	6/6	6/6	N	N	17	12	7	8	7
60	GK	22	2	5	110	70	24	99	85	6/6	6/6	N	N	16	13	9	10	11
61	D	26	2	5	80	90	21	97	85	6/6	6/6	N	N	11	17	8	9	15
62	AS	20	1	5	100	80	20	98	84	6/6	6/6	N	N	17	16	4	3	5
63	AS	20	1	5	120	80	24	98	85	6/6	6/6	N	N	13	12	7	8	10
64	AK	20	2	5	100	80	20	99	83	6/6	6/6	N	N	11	17	9	10	12
65	AS	21	2	5	120	70	21	97	85	6/6	6/6	N	N	21	16	10	9	14
66	AK	15	2	3	100	80	26	98	84	6/6	6/6	N	N	17	11	7	8	10
67	A	21	2	5	120	80	24	99	85	6/6	6/6	N	N	13	17	6	8	10
68	A	21	2	5	110	70	21	97	85	6/6	6/6	N	N	12	16	4	7	10
69	AN	20	2	5	100	80	22	98	84	6/6	6/6	N	N	17	13	10	9	8
70	N	19	1	5	120	70	24	99	85	6/6	6/6	N	N	11	17	8	11	10
71	HR	20	1	5	120	80	20	98	85	6/6	6/6	N	N	16	21	4	6	8
72	H	22	1	5	100	80	21	97	84	6/6	6/6	N	N	17	13	6	10	10
73	H	21	2	5	120	70	24	99	85	6/6	6/6	N	N	17	16	10	8	9
74	AK	20	2	5	100	80	26	98	84	6/6	6/6	N	N	15	17	8	9	10
75	A	20	1	5	120	80	21	98	85	6/6	6/6	N	N	17	13	9	10	12
76	A	28	2	5	90	60	24	99	83	6/6	6/6	N	N	16	16	10	9	10
77	AK	23	2	5	110	70	22	97	84	6/6	6/6	N	N	21	17	6	8	12
78	B	19	2	5	110	90	20	96	85	6/6	6/6	N	N	12	11	9	8	10
79	AS	13	1	3	120	80	24	99	84	6/6	6/6	N	N	17	16	10	9	10
80	A	20	2	5	110	70	21	98	85	6/6	6/6	N	N	12	17	8	10	12
81	D	20	2	5	100	80	26	99	84	6/6	6/6	N	N	17	11	9	10	12
82	D	20	2	5	120	70	24	98	84	6/6	6/6	N	N	16	17	10	7	8
83	M	13	1	3	110	90	21	99	83	6/6	6/6	N	N	17	12	8	9	10
84	M	25	2	5	110	70	20	99	85	6/6	6/6	N	N	21	13	10	12	15
85	D	19	2	5	120	80	24	98	84	6/6	6/6	N	N	17	16	6	8	10

S. No.		OCT Features											
	SCHIRMER(L/E)	CMT(R/E)	CMT(L/E)	GLT(R/E)	GLT(L/E)	RNFL(S)(R/E)	RNFL(S)(L/E)	RNFL(I)(R/E)	RNFL(I)(L/E)	RNFL(T)(R/E)	RNFL(T)(L/E)	RNFL(N)(R/E)	RNFL(N)(L/E)
45	12	257	263	76	78	126	147	147	152	73	63	64	62
46	15	274	278	87	87	134	125	146	146	78	72	64	59
47	13	246	245	82	84	112	117	118	100	60	59	70	66
48	10	196	216	86	86	114	123	120	107	55	52	70	66
49	9	235	232	82	78	115	113	124	118	58	66	72	49
50	10	244	241	83	84	124	131	110	124	73	60	58	71
51	8	220	217	87	87	122	138	137	142	74	80	64	75
52	9	233	228	87	88	121	136	121	126	57	57	66	66
53	10	210	206	74	74	112	97	102	115	66	61	71	72
54	9	204	191	85	83	106	111	91	101	60	53	61	60
55	10	252	249	92	95	157	156	133	134	69	71	95	95
56	9	265	258	84	80	127	130	133	127	56	54	68	61
57	9	261	258	82	82	140	151	136	138	61	56	84	62
58	8	251	253	92	90	136	120	106	103	60	68	87	87
59	8	219	185	85	100	143	99	138	153	68	58	78	69
60	10	222	228	81	83	115	109	116	114	64	53	60	61
61	10	267	267	77	75	115	114	104	91	63	62	56	60
62	6	216	215	73	73	109	95	112	118	56	58	66	53
63	12	228	219	84	83	105	111	123	112	65	64	63	57
64	15	250	246	92	90	128	136	127	151	69	71	89	79
65	12	218	219	80	80	128	120	147	138	48	48	86	89
66	8	253	243	88	89	122	152	158	164	70	62	74	87
67	9	237	237	87	88	109	119	118	117	77	68	70	80
68	9	253	259	87	89	122	142	111	128	59	54	89	88
69	9	233	233	79	79	122	128	114	116	56	56	56	56
70	9	253	255	82	82	114	117	124	124	54	57	81	69
71	9	222	234	76	80	141	118	134	130	66	59	54	55
72	7	249	240	77	75	113	106	110	114	56	56	77	68
73	8	223	227	96	96	136	111	136	130	64	63	105	88
74	9	248	236	80	79	102	98	108	114	62	61	63	82
75	11	230	226	77	77	101	106	99	105	67	67	68	58
76	12	247	246	83	85	118	132	116	116	72	66	77	81
77	10	263	240	85	90	107	118	124	107	65	65	66	74
78	8	247	244	80	81	138	149	153	143	55	58	85	79
79	9	259	253	83	85	122	114	106	107	77	72	70	83
80	10	257	257	86	87	113	105	119	119	81	72	58	57
81	10	257	254	85	83	131	148	136	123	75	70	64	61
82	8	223	223	82	83	132	135	118	121	45	47	84	72
83	9	249	246	80	81	107	116	128	132	51	48	76	74
84	14	214	217	78	78	108	103	121	118	57	56	70	67
85	12	235	229	78	80	95	106	114	112	58	57	61	60

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Subject:: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Yesha Gupta**, a student of your college for **MS Ophthalmology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
To measure retinal nerve fibre layer thickness in transfusion dependent thalassemia patients .

Supervisor	Co-Supervisor:-	Co-Supervisor:-
Dr. Sumeet Chopra	Dr. Shruti Kakkar	Dr. Ritesh Verma
Prof. & Head,	Assoc. Prof.,	Asst. Professor
Dept. of Ophthalmology	Dept. of Paediatrics	Dept. of Ophthalmology

The student may submit the thesis in triplicate alongwith the plan in triplicate also, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

TO MEASURE RETINAL NERVE FIBRE LAYER THICKNESS IN TRANFUSION DEPENDENT THALASSEMIA PATIENTS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MS

In

OPHTHALMOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

AUGUST, 2022

DR. YESHA GUPTA

DEPARTMENT OF OPHTHALMOLOGY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	TO MEASURE RETINAL NERVE FIBRE LAYER THICKNESS IN TRANFUSION DEPENDENT THALASSEMIA PATIENTS
For the degree of	MS(Ophthalmology)
Name of the candidate	Dr. Yesha Gupta
Supervisor	Dr. Sumeet Chopra, Professor and Head, Department of Ophthalmology, DMCH, Ludhiana
Co-Supervisor	Dr. Shruti Kakkar, Associate Professor, Department of Paediatrics, DMCH, Ludhiana Dr Ritesh Verma, Assistant Professor, Department of Ophthalmology, DMCH, Ludhiana
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INTRODUCTION

Beta thalassemia, an inherited coagulopathy can present with various ocular and systemic manifestations. Various ocular manifestations include tear film instability, pseudoxanthoma elasticum, angiod streaks, lenticular opacites and retinal nerve fibre layer thinning [a less elucidated one]. To measure retinal nerve fibre layer thickness we use Optical Coherence Topography [OCT].

AIM OF STUDY

1. To measure the retinal nerve fibre layer thickness using OCT in transfusion dependent thalassemia patients.
2. To compare retinal nerve fibre thickness in thalassemia patients to that of normal subjects.
3. To correlate the thinning with systemic parameters.

Materials and Methods

A cross sectional study including 85 subjects and 85 controls and measuring their retinal nerve fibre thickness using OCT in department of ophthalmology, Dayanand Medical College, Ludhiana

Keywords: Beta thalassemia, OCT, RNFL Thickness

(Signature) Candidate	(Signature) Co-supervisor	(Signature) Co-supervisor	(Signature) Supervisor	(Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"TO MEASURE RETINAL NERVE FIBRE LAYER THICKNESS IN TRANSFUSION DEPENDENT THALASSEMIA PATIENTS"** exist in the Department of Ophthalmology at Dayanand Medical College and Hospital, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate herself under our supervision and guidance.

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APPROVAL PROFORMA
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Department	Ophthalmology
Topic of Thesis	TO MEASURE RETINAL NERVE FIBRE LAYER THICKNESS IN TRANSFUSION DEPENDENT THALASSEMIA PATIENTS
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PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

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4	DATE OF ADMISSION OF COURSE	07/03/2022
5	TITLE OF THE TOPIC	TO MEASURE RETINAL NERVE FIBRE LAYER IN PATIENTS WITH TRANSFUSION DEPENDENT THALASSEMIA PATIENTS

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Thalassemia's are a common cause of hypochromic microcytic anemia which arises from the reduced or absent synthesis of the globin chain of hemoglobin [Hb]. Thalassemia's are a quantitative defect of hemoglobin synthesis. Beta-thalassemia refers to an inherited mutation of the beta-globin gene, causing a reduced beta-globin chain of Hb.[1]

There are three classifications of thalassemia- thalassemia minor, thalassemia intermedia and thalassemia major [TM]. Thalassemia minor is usually mild but the other two are distinguished clinically by transfusion dependence. TM requires routine transfusions, and intermedia does not.[2]

Clinical Diagnosis

TM is usually suspected in an infant younger than two years of age with severe microcytic anaemia, mild jaundice and hepatosplenomegaly. Thalassemia intermedia presents at a later age with similar but milder clinical findings. Carriers are usually asymptomatic, but sometimes may have mild anaemia.

Hematologic Diagnosis

Red blood cell [RBC] indices show microcytic anaemia. TM is characterized by reduced Hb level (<7 g/dl). Thalassemia intermedia is characterized by Hb level between 7 and 10 g/dl. Thalassemia minor is characterized by reduced MCV and MCH, with increased HbA_2 level.[2]

SYSTEMIC COURSE

In some developing countries, where due to the lack of resources patients are untreated or poorly transfused, the clinical picture of TM is characterized by growth retardation, pallor, jaundice, poor musculature, genu valgum, hepatosplenomegaly, leg ulcers, development of masses from extramedullary haematopoiesis, and skeletal changes resulting from expansion of the bone marrow.

COMPLICATIONS

Complications are related to overstimulation of bone marrow, ineffective erythropoiesis, and iron overload from blood transfusions.

Iron accumulates in the heart, causing heart failure, which is the most common cause of death in TM due to iron accumulation. Usually, these patients have dyspnea, with resting tachycardia, low blood pressure, high ejection fraction, and high cardiac output [3]. Atrial fibrillation [4] is another long-term complication of iron oxidative stress.

Iron also accumulates in endocrine glands causing hypothyroidism, hypoparathyroidism, adrenal insufficiency, diabetes mellitus, and hypogonadism.

Thromboembolic events such as deep venous thrombosis, pulmonary embolism, and recurrent arterial occlusion are common. [5].

Other complications are chronic hepatitis (from blood transfusion infection of hepatitis B and C viruses), cirrhosis (iron overload), hypersplenism, HIV infection, and osteoporosis [2].

OCULAR MANIFESTATIONS OF BETA THALASSEMIA

Frequency of ocular involvement differs among various studies. Ocular findings in beta-thalassemia may correlate to the disease itself, iron overload or the chelating agents used. Ocular manifestations include ocular surface disease, lens opacities and retinal pigment epithelium [RPE] degeneration. [6]

Ocular surface disease

Ocular surface disease as demonstrated by alterations in tear function parameters (reduced tear film break up time [TBUT], reduced Schirmer test values) has been attributed to goblet cell loss as well as squamous metaplasia of the conjunctiva, possibly due to reduced anti antioxidants. Thalassemia patients seem to be more vulnerable to UV radiation through peroxidative tissue injury because of secondary iron overload caused by lifelong blood transfusions.[7]

Anterior segment abnormalities

Lens opacities are one of the most important factors for the reduction of visual acuity in children with TM and may interfere with vision if they are near the visual axis [6].

Fundus changes

Fundus changes in TM are frequent, age-dependent, and similar to those reported for Pseudoxanthoma elasticum [PXE] except for the

presence of retinal vascular tortuosity. Because these changes, in particular angioid streaks and pattern dystrophy-like changes, these are well known to predispose to sight-threatening complications such as Choroidal Neovascularization (CNV), hence regular ocular check-ups are essential [8].

PXE-like fundus changes

The term PXE-like syndrome has been used to describe vascular, dermal and ocular alterations characteristic of PXE that occur secondary to other diseases or due to genetic mutations different from those in PXE and these can be seen in various haemoglobinopathies including TM [9]. PXE-associated fundus changes consist of peau d'orange encompassing the circular periphery, comet tail lesions within the periphery and central pattern dystrophy-like changes. Optic disc drusen are not pathognomonic but a frequent finding.[10]

Deferrioxamine retinopathy

Desferrioxamine[DFO] is an iron chelating agent used in the treatment of chronic iron overload in patients with TM.

Ocular findings in fundoscopy vary and may include RPE opacification or loss of transparency, foveomacular, macular, paramacular, papillary or peripapillary and peripheral degeneration or combination of these. RPE pigment changes, optic disc edema and optic atrophy can also be seen.

DFO should be promptly discontinued in symptomatic patients without life-threatening iron overload because of the likelihood of further worsening. [11,12]

In view of wide array of changes seen in the eye of the patient, RNFL thinning remains an unexplored area of field and need to be studied.

The best tool to study retinal nerve fibre layer thickness is the OCT.

6.2 REVIEW OF LITERATURE

UZUN ET AL [15]-compared 47 patients of TM with 51 controls. Each subject underwent a standard ophthalmological examination. The mean age of the patient group and healthy controls were 13.7 ± 2.1 and 14.3 ± 2.2 years, respectively in this study. Mean peripapillary RNFL thickness was 94 µm in the TM group, and 100 µm in the control group ($p < 0.01$). In patients with TM, RNFL was thinner in all quadrants than control subjects. Within the TM group neither average RNFLT nor each four quadrant RNFLT were correlated with the age, serum ferritin or serum Hb levels ($p > 0.05$). In this study, it was observed that RNFL was thinner in patients with TM. Thinning of RNFL did not correlate with Hb or ferritin levels.

Similarly, ***BASIONY ET AL*** [16] did a cross-sectional study that included 15 patients with TM and 15 healthy children as a control group, who were recruited from the Pediatric Department, Menoufia University Hospital, Shebin El Kom, Menoufia, Egypt, from March 2020 to December 2020. All children were subjected to a standard ophthalmological examination. The mean Hb level was statistically significantly less in the TM group (6.79±0.69 g/dl) compared with the control group (13.67±0.57 g/dl) ($P<0.001$). The serum ferritin level was significantly increased among the TM group (4280.0±1250.83 ng/ml) compared with the control group (60.70±92.46 ng/ml) ($P<0.001$). The mean blood transfusion history among patients with TM was 1.07±3.37/month. In this study it was found that the nasal superior, nasal inferior, and nasal sectors were significantly thinner in patients with TM than in the control group ($P<0.05$). In patients with TM, the average RNFLT and each individual quadrant RNFLT (temporal, temporal inferior, and nasal inferior) were not statistically significantly correlated with serum ferritin and serum Hb($P>0.05$). On the contrary, the nasal superior sector was significantly correlated with serum Hb, whereas the temporal superior and nasal sectors were significantly correlated with serum ferritin ($P<0.05$).

It was found that the RNFL was thinner in patients with TM compared with the control group. The RNFL thickness was correlated positively with the decreasing Hb level.

AKSOY ET AL [17]- measured peripapillary RNFLT in children with TM, children with iron deficiency anaemia (IDA), and children in a healthy control group. In this study**,** a total of 47 children with TM and 22 children with IDA were selected from two paediatric haematology outpatient clinics as our experimental groups, while 35 healthy children were randomly selected from a primary school to act as a control group. After a complete eye examination was conducted and intraocular pressure measurements were obtained, RNFL measurements were performed using OCT. The mean age of the participants was 9.65 ± 4.13 years in the TM group, 9.14 ± 2.53 years in the IDA group, and 9.13 ± 3.29 years in the control group, respectively, with no statistically significant difference among the three groups ($p > 0.05$). Mean peripapillary RNFL Thickness was 119.38 ± 35.49 microns in the TM group, 184.00 ± 31.14 microns in the IDA group, and 187.73 ± 27.36 microns in the control group. was significantly thinner in all quadrants in the TM group vs. the other two groups ($p < 0.01$), and in only the inferior quadrant in the IDA group ($p < 0.05$). Average RNLFL thickness correlated positively with mean Hb value ($r = 0.488$; $p < 0.001$) and negatively with mean ferritin level ($r = -0.544$; $p < 0.001$), but no correlations with mean number of transfusions and mean visual acuity were observed ($p > 0.05$). The study revealed that peripapillary RNFL is thinner in TM in all quadrants and in only the inferior quadrant in IDA. Thinning of the RNLFL correlated with haemoglobin value and ferritin level, but not with number of transfusions and visual acuity.

Refractive status differences between TM patients and healthy controls, are not consistent among studies. ***Nowroozzadeh***[18] reported that children with TM had higher percentage in terms of against the rule astigmatism (typically corneal and lenticular astigmatism) and shorter axial length .

Significant correlation of lens opacities with higher average serum iron levels, ferritin levels and number of blood transfusions received (*P* <0.001), has been reported by ***Taneja*** [19]. Iron-chelating agents have also been implicated as causative agents of lens opacities. Although a correlation between occurrence of lens opacities and dose of deferoxamine received has not been established. Oxidative damage of the lens by iron overload or disturbance of oxidant/antioxidant balance may be a causative factor of lens opacities in beta-thalassemia patients.

DE VIRGILIIS, did a prospective study involving fifteen children, aged from 9 to 16 years, with transfusion dependent TM and moderate iron overload (serum ferritin concentra- tions from 1100 to 2000 [tg/l), because of low compliance with daily infusion of subcutaneous desferrioxamine, were treated by a combination of traditional daily subcutaneous infusion and monthly intravenous administration of very large doses. Each patient was treated for 10 consecutive months. The dose of desferrioxamine for subcutaneous infusion was 40-60 mg/kg over a period of 12 hours each night for six days a week. The intravenous infusion was given over a period of 24 hours at the dosage of 10-12 g (200-450 mg/kg) dissolved in 750 ml of 5% glucose solution. Ophthalmic evaluation was carried out before and after the termination of the infusion, but this assessment was repeated from two to three times at times of successive intravenous infusion and again one, two, and three months after inter- rupting the intravenous infusions while continuing the subcutaneous administration. This study showed that high doses of intravenous desferrioxamine infused over a short period produce a reversible minor toxic effect on the retina, which is characterised by reduced amplitude on adapted electroretinography and defective dark adaptation. More severe retinal or optic nerve toxicity, or both, that consisted of night blindness, field defects, visual loss, loss of colour vision, and delayed visual evoked potential was detected after intra- venous or subcutaneous infusion of similar large doses of desferrioxamine for a prolonged period. Follow up studies in some of these patients showed evidence of evolution towards the

pigmentary degeneration of the retina indicating toxicity at the level of retinal pigment epithelium.[12]

6.3 AIMS AND OBJECTIVE

1. To measure the retinal nerve fibre layer thickness using OCT in transfusion dependent thalassemia patients.
2. To compare retinal nerve fibre thickness in thalassemia patients to that of normal subjects.
3. To correlate the thinning with systemic parameters.

7. MATERIAL AND METHODS

7.1 SOURCE OF DATA

TYPE OF STUDY-Cross sectional study with case and control groups

STUDY POPULATION-

To calculate the sample size of the study,

The formula used is as under:

$n = (\sigma 12 + \sigma 22) (Z\alpha + Z\beta)^2/(m1 – m2)^2$

Where,

Zα = Value of standard normal variate corresponding to α level of significance (1.96)

Zβ = The standard normal deviate for desired power (0.842)

m = mean

σ = Standard deviation

Assumptions:

From the study conducted by UZUN ET AL

Mean Group (m1) = 94

Mean Group (m2) = 100

Coefficient of variation = 150%

Standard deviation Group (σ1) = 10

Standard deviation (σ2) = 17

With the above assumptions the sample size for 95% confidence level & 80% power works out 85 in each group

HENCE CASE GROUP-85 CONTROL GROUP-85

INCLUSION CRITERIA-

1. Any patient willing to participate in the study.
2. K/C/O transfusion dependent thalassemia at thalassemia day care center, Dayanand medical college, Ludhiana.
3. Age between 5 and 30 years of age.
4. Patients cooperating for OCT.

EXCLUSION CRITERIA-

1.Children with history of retinal diseases.

2. Children with Type -1 diabetes mellitus.

3.Children with history of any intraocular surgery.

4. Children with optic disc disorders.

5.Children with history of retinopathy of prematurity.

7.2 METHODS OF COLLECTION OF DATA

A total of 170 subjects (340 eyes) will be evaluated in the study and patients will be divided in two groups according to their refractive status: Group 1 – pre-diagnosed cases of TM and Group 2- controls

All subjects will undergo comprehensive ophthalmic evaluation which include visual acuity measurement by Snellen's chart, slit lamp examination, non- contact tonometry, fundus examination by indirect ophthalmoscopy. Before testing, the pupil of each subject will be dilated by instillation of 1% tropicamide and 2.5% phenylephrine hydrochloride to the eye three times over a 10 minutes period. Peripapillary RNFL thickness will be measured using ZEISS CIRRUS OCT machine.

PRINCIPLE OF OPTICAL COHERENCE TOMOGRAPHY

OCT is a quick, non-invasive and reproducible imaging tool for macular lesions and has become an essential part of clinical practice.

OCT is an optical analog of ultrasound imaging that uses low coherence interferometry to produce cross-sectional images of the retina. It captures optical scattering from the tissue to decode spatial details of tissue microstructures. It uses infrared light from a super-luminescent diode that is divided into two parts: one of which is reflected from a reference mirror and the other is scattered from the biological tissue. The two reflected beams of light are made to produce interference patterns to obtain the echo time delay and their amplitude information that makes up an A-Scan. [13.14]

A minimum pupil diameter of 3 mm is required to obtain a good OCT image. An appropriate scanning protocol is selected to scan the retinal area of interest and a live OCT window is seen. The patient is instructed to look at the internal target at the centre (for macular scanning) or an external target where appropriate. Once the fundus image on the monitor is focused, the OCT image appears on the

monitor, focus is enabled by correcting refractive errors. The saved OCT scans are analysed both qualitatively and quantitatively. The OCT view window consists of the analysed OCT images with its corresponding fundus image showing the orientation of the OCT scan. The analysis report varies with different OCT systems. Warm colours indicate thicker retinal areas and cool colours indicate thinner retinal areas.

The subject will be seated and aligned properly, three 200x 200-cube optic disk scans will be obtained per eye, scans with poor signal strength will be discarded, and new one will be obtained. All scans will be performed by a single operator. The average RNFL thickness, the average thickness in the four sectors — superior, inferior, temporal and nasal and the average thickness in all clock hour positions will be recorded. The superior clock hour will be 12 o'clock, and the others will be assigned accordingly in a clockwise manner in the right eye and counterclockwise in the left.

OUTCOME

Outcome will be measured in terms of retinal nerve fibre layer thickness, central macular thickness and ganglion layer thickness.

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. To determine whether the data is normally distributed, a Kolmogorov-Smirnov test will be used. Comparison of quantitative variables between the study groups will be done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square ($\chi 2$) test will be performed and fisher exact test will be used when the expected frequency is less than 5. A probability value (p value) less than 0.05 will be considered statistically significant. All statistical calculations will be done using

(Statistical Package for the Social Science) SPSS 21 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Yes, investigation to be used is OCT [quick and non-invasive optical analog of ultrasound imaging]

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes, Attached herewith

8. LIST OF REFERENCES

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PATIENT PERFORMA

S.no **Name** **Age**

MRD

Address **Ph.NO** **Education-**

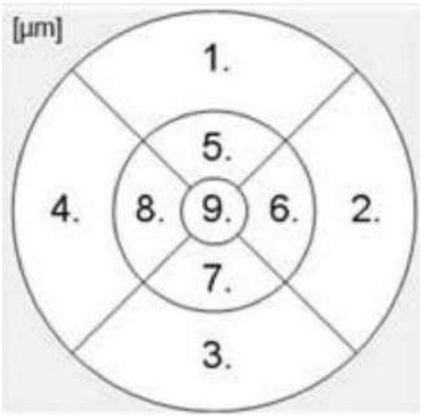
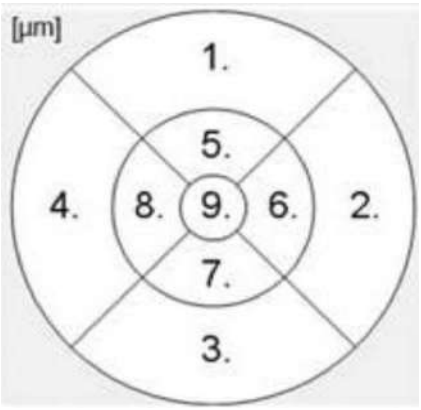
Date of enrolment-

Date of data entry-

Vitals-		
Blood pressure		
Respiratory rate		
Oxygen saturation		
Heart Rate		
Age at diagnosis		
History of consanguinity		
Any systemic co-morbidity		
Age of initiating transfusion		
Age of initiating chelation		
Type of chelation	A] DESFEROXAMINE	
	B] DEFERIPRONE	
	C]DEFERASIROX	
	D]DESFEROXAMINE+DEFERIPRONE	
	E] DEFERIPRONE + DEFERASIROX	
	F] DESFEROXAMINE+DEFERASIROX	
Duration of chelation [in patient years of exposure]		
Average haemoglobin in thalassemia patients over 5 years		
Average transfusion requirement in thalassemia patients over 5 years		

Signature of Candidate **Signature of Supervisor**

Co- existent endocrinal disorder	[A]HYPOTHYROIDISM	
	[B]HYPOPARATHYROIDISM	
	[C]DIABETES MELLITUS	
	[D]SHORT STATURE	
	[E]DELAYED PUBERTY	
Co-existent infection (In thalassemia patient)	[A]HEPATITIS -B	
	[B]HEPATITIS-C	
	[C]HIV	
Serum ferritin levels (In thalassemia patients)		
Liver iron concentration [LIC] (In thalassemia patients)		
Cardiac MRI [T2] (If available)		
Best corrected visual acuity	R/E	L/E
Colour vision	R/E	L/E
Intra ocular pressure [using non-contact tonometer]	R/E	L/E
Tear film break up time	R/E	L/E
Schirmer	R/E	L/E
Slit lamp examination	R/E	L/E
OCT parameters-		

Retinal nerve fibre layer thickness		
Central macular thickness		
Ganglion layer thickness		

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I…… D/o, W/o, S/o……..…… am willing to participate in the study **"TO MEASURE RETINAL NERVE FIBRE LAYER THICKNESS IN TRANSFUSION DEPENDENT THALASSEMIA PATIENTS"** The investigation has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

……. ……
Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य "**TO MEASURE RETINAL NERVE FIBRE LAYER THICKNESS IN TRANSFUSION DEPENDENT THALASSEMIA PATIENTS"**में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____	_____
गवाह के हस्ताक्षर	रोगी के हस्ताक्षर/अंगूठे का निशान
नाम:	नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

“ TO MEASURE RETINAL NERVE FIBRE LAYER THICKNESS IN TRANSFUSION DEPENDENT THALASSEMIA PATIENTS” ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ